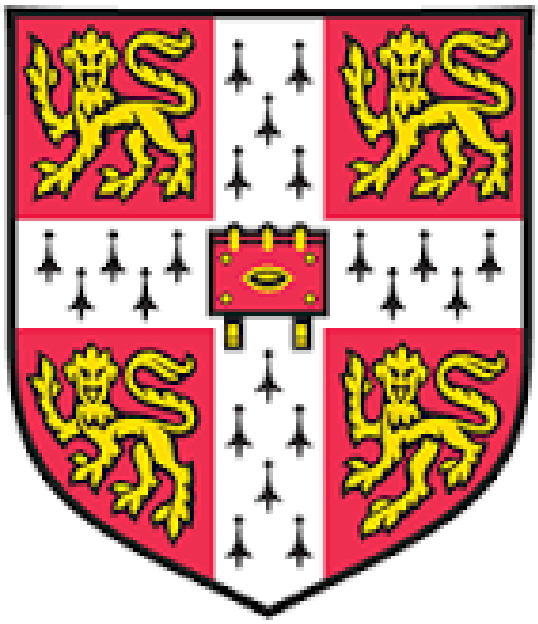
Loneliness in the Oldest Old



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This dissertation is submitted for the degree of Doctor of Philosophy
October 2018

Declaration

This dissertation is the result of my own work and includes nothing which is the outcome of work done in collaboration except as declared in the Preface and specified in the text. It is not substantially the same as any that I have submitted, or, is being concurrently submitted for a degree or diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text. I further state that no substantial part of my dissertation has already been submitted, or, is being concurrently submitted for any such degree, diploma or other qualification at the University of Cambridge or any other University or similar institution except as declared in the Preface and specified in the text.

The thesis does not exceed the 60,000 word limit, excluding tables, figures, appendices and references, set by the degree committee of the School of Clinical Medicine.

Thesis summary

Loneliness in the Oldest Old

Hanyuying Wang

The importance of social relationships for health in later life has been explored over the past decades. Loneliness has been found to be an adversity associated with ageing. People who feel lonely are at greater risk of experiencing increased morbidity and mortality. However, the existing evidence on the determinants of loneliness as well as the effects of loneliness on health are exclusively based on relatively young-old people (65 years and over) with the oldest old (80 years and over) under-represented. Compared to the young-old people, the oldest old are more likely to experience health problems and have fewer ties or contacts with others; therefore, they might be more likely to suffer from loneliness. This thesis aims to investigate loneliness in the oldest old. Specific thesis objectives are (1) exploring the individual-level determinants of loneliness, identifying how patterns of loneliness change with age and the individual-level factors associated with loneliness transitions; (2) investigating the effects of loneliness on health (i.e. all-cause mortality and cognitive decline); and (3) examining the relationship between loneliness and health service and social care utilisation.

In order to investigate the objectives, data from the Cambridge City over 75s Cohort (CC75C) study were used. The CC75C study is a population-based study of the very old. It started in 1985, surveying a representative sample of men and women aged 75 years or older living in Cambridge. Partial proportional odds model and multi-state modelling were used to explore the determinants of loneliness, identify the changing patterns of loneliness as well as examine the risk factors associated with loneliness transitions. Cox regression models and generalized estimating equations (GEE) were used to explore the effects of loneliness on all-cause mortality, cognitive decline, and health service and social care utilisation, respectively. The findings reveal clear associations between loneliness and all-cause mortality, cognitive function, as well as health and social care service use of the oldest old, possible mechanisms and the importance of developing societal approaches to alleviate loneliness.

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Acknowledgements

First and foremost, I would like to express my thanks to my supervisor, Professor Carol Brayne, who has patiently guided me through my Ph.D. journey. I always feel lucky to have a very helpful, understanding and supportive supervisor.

I am grateful to my advisors, Professor Kay-Tee Khaw and Dr. Jane Fleming, for their constant encouragements and invaluable comments on my research projects. I would like to thank Professor Fiona Matthews for her important advice on statistical analyses. My gratitude goes to Professor Tom Dening, Ms. Sally Hunter, Dr. Yue Leng, Dr. Yu-Tzu Wu, Ph.D. student Zhirong Yang, and Mr. Sebastian Walsh for giving me early feedback on my work. I also would like to thank Dr. Louise Lafortune for her generous invitation to a conference.

My appreciation extends to everyone who supported and helped with the development of the CC75C study; this includes the CC75C staff, the participants, their families, GPs and the project funders.

I would like to thank colleagues in the office. Special thanks to Ms. Judith Willows and Ms. Sabina Taylor for their countless help on academic related matters. My gratitude goes to Sarah Assaad, Olivia Remes, Holly Bennett, Justin Yang and Richard Merrick, with whom I have always had enjoyable conversations. I am also grateful to Meg Westbury, the librarian and fellow at Wolfson College, for her general advice on article searching.

Finally, I would like to express my thanks to my family and friends. Special thanks go to Zheng Yuan and Chen Gao for always being there whenever I need “an ear”. I would like to acknowledge my husband for his patience, love and encouragement. Words are powerless to describe my appreciation and gratitude to my parents, Guangyan Yao and Yubao Wang, for all the sacrifices that they have made on my behalf. Without their unconditional love and support, I would not have been able to get this far. I will continue to grow and become a better person with their love, support and guidance.

Publications & Conferences

Articles Published

Wang, H., Leng, Y., Zhao, E., Fleming, J., Brayne, C., & CC75C Study Collaboration. (2018). Mortality risk of loneliness in the oldest old over a 10-year follow-up. *Aging & mental health*, 1-6.

Wang, H., Fleming, J., Brayne, C., Zhao, E., Dening, T., & Khaw, K. T. (2019). Is loneliness associated with increased health and social care utilisation in the oldest old? Findings from a population-based longitudinal study. *BMJ Open 2019;9:e024645. doi: 10.1136/bmjopen-2018-024645*

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Article accepted

Wang, H., Fleming, J., Dening, T., Hunter, S., Khaw, K. T., Brayne, C. (accepted). Longitudinal analysis of the impact of loneliness on cognitive function over a 20-year follow-up. *Aging & Mental Health.*

Article submitted

Wang, H., Walsh, S., Yang, Z. R., Brayne, C. (submitted). Loneliness and health service and social care usage: a systematic review.

Articles in preparation

Wang, H., Yang, Z.R., Fleming, J., Khaw, K.T., Brayne, C. (in preparation). Cross-cultural perspectives of loneliness: laypeople's perspectives of loneliness in the UK and China.

Conference abstracts

Wang, H., Fleming, J., Brayne, C. (2017). The prevalence of loneliness in the oldest old aged over 80: the Cambridge City over 75s Cohort study. Poster presentation, Emerging Researchers Conference "Demography, Ageing and Health", Oxford.

Wang, H., Fleming, J., Brayne, C. (2018). Is loneliness associated with cognitive decline? Findings from a population-based longitudinal study. Poster presentation, Public health showcase, Cambridge.

Wang, H. & Brayne, C. (2018). The social determinants of loneliness in the oldest old. Poster presentation, Wolfson College Research Event, Cambridge.

Wang, H., Leng, Y., Brayne, C. (2018). Changes in loneliness over time in the oldest old. Poster presentation, Loneliness in Older People and its Impact on Health, British Geriatrics Society, London.

Wang, H., Leng, Y., Fleming, J., Brayne, C. (2018). The impact of loneliness on all-cause mortality in the oldest old. Poster presentation, The Faculty of the Psychology of Older People Annual Conference, Cambridge.

Wang, H., Fleming, J., Khay, K. T., Brayne, C. (2018). Is loneliness associated with increased demands for health and social care services? Oral presentation, Ageing & Society: Eighth Interdisciplinary Conference, Japan.

Chapter 1 Introduction

1.1 Social relationships

"…my father told me of a careful observer, who certainly had heart-disease and died from it, and who positively stated that his pulse was habitually irregular to an extreme degree; yet to his great disappointment it invariably became regular as soon as my father entered the room." – Charles Darwin (Expression of the Emotions in Man and Animals, 1872).

1.1.1 Definition

"A social relationship is characterized by at least a minimum of mutual orientation of the action of each to that of the others. Its content may be of the most varied nature: conflict, hostility, sexual attraction, friendship, loyalty, or economic exchange. […] Hence, the definition does not specify whether the relation of the actors is co-operative or the opposite" (Max Weber, 1978, p.27). According to this definition, the nature of social relationships is that relationships involve more than one individual; that there must be mutual influences existing between individuals; and that the influences can be positive and negative. In other words, social relationship is the degree to which an individual is connected to, and embedded in, a society (or societies). Therefore, social relationship is a multi-dimensional term and can take various forms. For instance, in the field of social epidemiology, when investigating the importance of social relationships in health, terms such as social integration, social support, social ties or social network are used, and most often are used loosely and interchangeably (Berkman and Kawachi, 2000).

1.1.2 A brief history of theoretical approach to social relationships

The importance of social relationships was first recognized in the 19th century by a French sociologist, Emile Durkheim, through his work on suicides. By observing and comparing suicide rates between people of different religions, between those who were married and unmarried, he concluded that "Suicide varies inversely with degree of integration of the social groups of which the individual forms a part" (Durkheim,

1897, 1951, p.209). This finding indicated that social structure and social integration have a role in influencing individuals' behaviours, and although it was primarily based on observations of suicide patterns. Durkheim paved the way for future researchers in this field.

In 1969, a psychiatrist, John Bowlby, developed attachment theory, which was considered to be another milestone in recognition of the importance of social relationships for well-being. Bowlby believed that social relationships developed in childhood, especially the natural bonds formed with their mothers, not only influence children's physical health during growth but also provide a psychological protection for their adulthood life (Bowlby, 1969). The strength of Bowlby's attachment theory lies in its life course perspective in understanding the impact of social relationships on individuals' development.

From 1970s to 1980s, an egocentric social network theory was developed by a group of sociologists (Wellman and Leighton, 1979; Fischer, 1982). According to this theory, an individual forms the centre of a network, and his or her connections with others form the structure of this network. The social network theory provides a means to quantify social relationships, such as by measuring the number of individuals within the network or the frequency of contacts (J.Cacioppo and S.Cacioppo, 2014). Based on this theory, a group of psychologists (Antonucci and Israel, 1986; Kahn, 1979; Lin and Dean, 1984; House, 1983) developed a social support theory that emphasizes the importance of social support on human development across life span. Cohen and Wills (1985) further categorized social support into two aspects: structural and functional. The structural aspect of social support refers to the quantitative perspective of social connections (e.g. number of social ties, marital status, number of children), while the functional aspect of social support refers to the qualitative perceptions of social connections (e.g. whether an individual is satisfied with the support they obtain from others).

Despite these theories, none fully capture multi-dimensions of social relationships or explain how they could affect health. To address this question, Berkman and Kawachi (2000) developed a more comprehensive framework of social relationships - the social epidemiological conceptual framework, in which a cascading causal process

from social networks to health is suggested (Figure 1.1). In general, a social network is influenced by the social structural conditions in which it is embedded, such as culture, socioeconomic factors and politics; it also provides opportunities for the development of psychosocial mechanisms through which social networks exert effects on health outcomes.

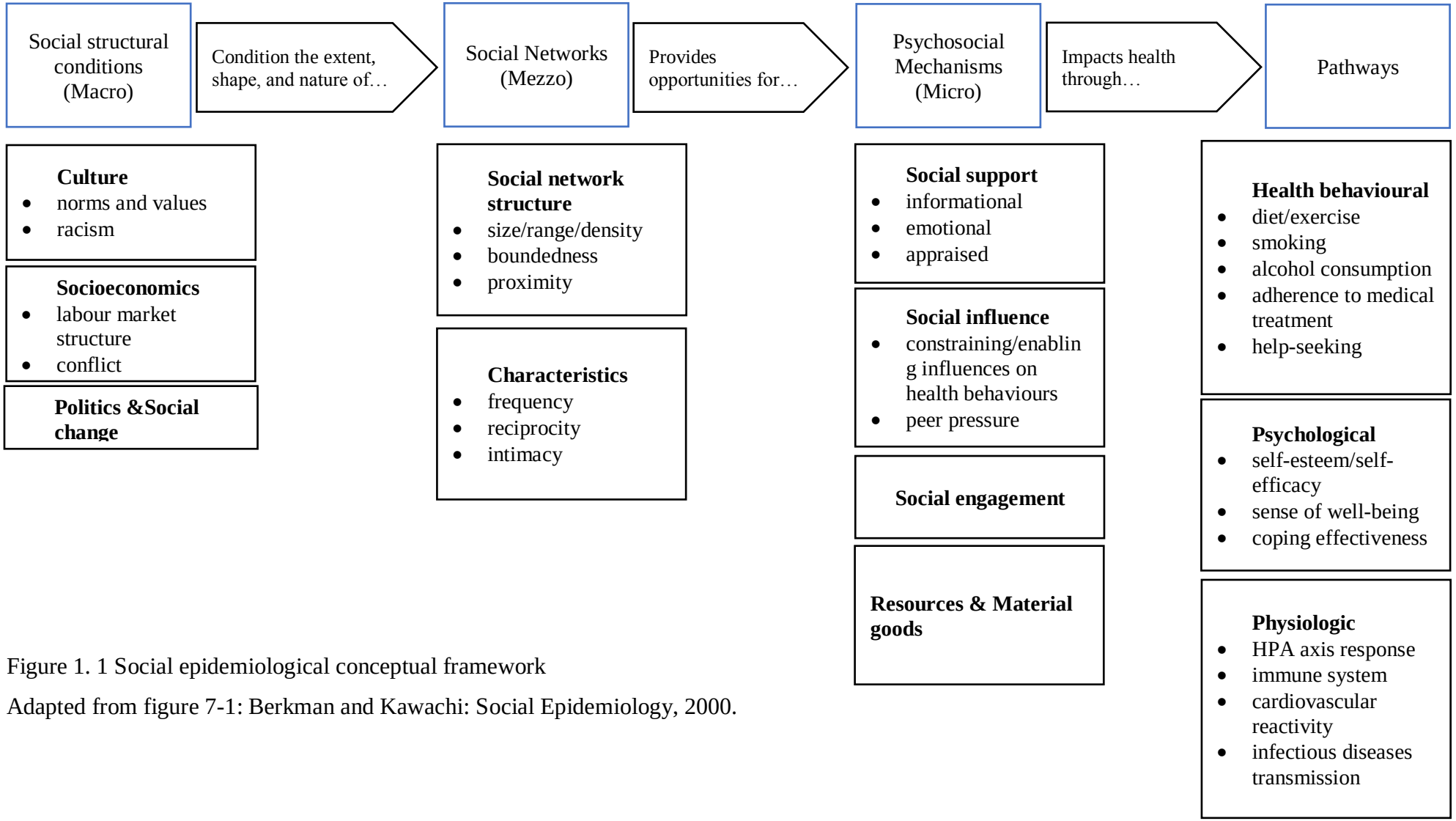


Figure 1. 1 Social epidemiological conceptual framework

Adapted from figure 7-1: Berkman and Kawachi: Social Epidemiology, 2000.

1.1.3 The importance of social relationships in modern society

Human beings are social animals. In ancient times, we relied on groups (i.e. social relationships) for survival and reproduction. In modern society, the significance of social relationships on health has been recognized (House et al, 1988a).

In 1974, Weiss proposed six types of 'provision' offered by social relationships: (1) attachment; influenced by Bowlby's attachment theory, Weiss believed that social relationships should provide individuals with a sense of security, warmth and love, (2) social integration, a sense of companionship or shared social norms and values, (3) reassurance of worth, a sense of being needed and valued, (4) reliable alliance, meaning the continuous assistance that individuals can obtain from social relationships, (5) guidance, trustworthy advice provided by social relationships and (6) opportunity for nurturance, indicating a realization that one should be responsible for others' well-being.

Since then, several other provisions have been developed (Cobb, 1979; Kahn, 1979; Schaefer et al., 1981; Cohen and Wills., 1985), but it seems that all are captured by Weiss's theory (Table 1.1). For instance, the reassurance of worth reflecting the sense of self-value and self-esteem mentioned in Weiss's social provision theory was classified as esteem support by Cobb (1979) and Cohen and Wills (1985), and affirmation by Kahn (1979).

Table 1. 1 Different components of social relationships

Weiss (1974)	Cobb (1979)	Kahn (1979)	Schaefer et al. (1981)	Cohen and Wills (1985)
Attachment	Emotional Support	Affect	Emotional Support	
Social Integration	Network Support			Belonging Support
Reassurance of Worth	Esteem Support	Affirmation		Self-esteem Support
Reliable Alliance	Material Support	Aid	Tangible Aid	Tangible Support
Guidance	Instrumental Support		Informational Support	Appraisal Support
Opportunity for Nurturance	Active Support			

Adopted from 'The provisions of social relationships and adaptation to stress' by Cutrona and Russell, 1983.

In conclusion, apart from providing fundamental support for human beings' survival and reproduction, social relationships also offer protection and support to be able to thrive at the individual and the collective level.

1.1.4 Social relationships and health

Given the importance of social relationships, it is not hard to assume that deficient social relationships will harm human beings' health. Empirical evidence has shown that lower levels of social integration and lower quality of social relationships are linked to later health deterioration (Seeman, 1996).

1.1.4.1 Social relationships and mortality

Evidence on the association between social relationships and mortality has been accumulating over the past 40 years. Longitudinal analyses have provided evidence that deficits in both quantitative (e.g. fewer social ties, fewer contacts, social isolation, etc.) and qualitative (e.g. unhappy marriage, lack of social support, bereavement, etc.) aspects of social relationships are associated with greater risk of mortality (Berkman and Syme, 1979; House et al., 1988a; Lichtenstein et al., 1998; Rosengren et al., 1993). A recent meta-analysis, after examining data from 148 studies, found that

stronger social relationships were associated with increased likelihood of survival (OR=1.5, 95% CI 1.4, 1.6) among older people. Moreover, this study also found that different types of social relationships, such as social integration, living arrangement, affected mortality risk independently after adjusting for socio-demographic factors, participants' health and study follow-up length (Holt-Lunstad et al., 2010).

1.1.4.2 Social relationships and morbidity

Studies on the effect of social relationships on health began to emerge soon after the development of the concept of social support. This supports a positive effect of social support on health (see reviews by Berkman, 1985; Cassel, 1976; Cohen, 1988; House et al., 1988b; Seeman, 1996). This finding was observed across studies with a wide range of health outcomes, including coronary heart disease (CHD), cancer, infectious diseases, anxiety and physiological arousal.

A more recent comprehensive systematic review of longitudinal cohort studies, drawing on data from 19 studies, identified low social participation, less frequent social contact and loneliness as being significantly associated with increased risk of incident dementia, and the strength of the associations was comparable with other well-known risk factors for dementia, such as low education attainment, physical inactivity and late-life depression (Kuiper et al., 2015).

1.1.5 Mechanisms underlying the association between social relationships and health

Several pathways have been proposed through which social relationships might exert effects on health. Broadly, these mechanisms can be characterised into two distinct models: the main-effect model and the stress-buffering model.

1.1.5.1 The main-effect model

The main effect model posits that social relationships have main or direct effects on health irrespective of the presence of stress (Cohen and Wills, 1985). According to this model, social relationships provide social influence (i.e. social norms and guidance that are commonly understood and accepted by individuals), provide and

transmit social resources (i.e. health related resources, such as health service information), and provide positive psychological responses (i.e. a sense of belonging, love, security, as well as recognition of self-worth). Such psychological responses may directly impact health, whereas social influence and social resources may influence individuals' health through influencing their health related behaviours (Figure 1.2). For example, if an individual is living in a society that has great awareness of the negative impact of smoking, then this individual is less likely to smoke cigarettes, therefore, he or she is less likely to develop smoking-related diseases.

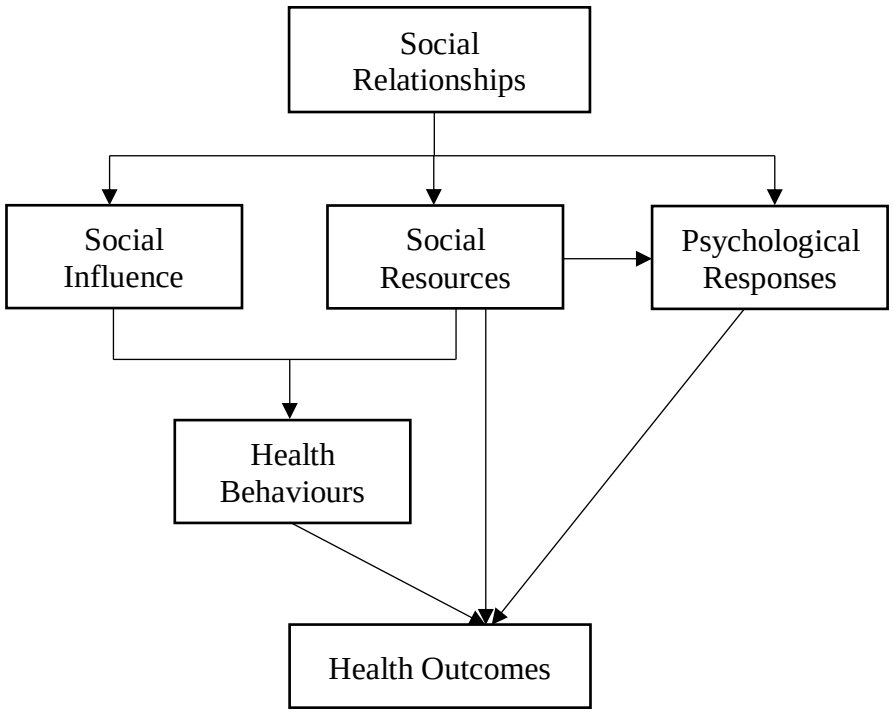


Figure 1. 2 The main-effect model

Adapted from Social Support Measurement and Intervention. A Guide for Health and Social Scientists. New York: Oxford University Press. Gottlieb et al., 2000.

1.1.5.2 The stress-buffering model

The stress-buffering model proposes that social support can act as a buffer to regulate the process of how stress influences health (Cohen and Wills, 1985). Potential stressful events may invoke subsequent appraisal responses through disturbing neuroendocrine and immune system functioning or discouraging individuals to seek help, which further influence health conditions. However, the presence of social support can re-define this process by either intervening in the appraisal reactions (here the appraisal reactions indicate that individuals may regard the stressful events as highly stressful or not stressful. The perception that others can provide help may increase individuals' confidence and bolster their perceived ability to cope with the stresses, therefore, preventing an event from being appraised as stressful) to a potential stressful event or intervening in the physiological responses which appraisal responses invoke (Figure 1.3). In particular, when potential stressful events occur, the perceived availability of social support can enhance individuals' capacity to cope with stress, turn potential stresses into un-stressful events, thus preventing subsequent negative responses. Additionally, in the downstream process, if potential negative events are considered stressful by individuals, the presence of social support can regulate physiological responses or encourage individuals to adapt proper behaviours to avoid potential damages on health. For example, if a smoker wants to quit smoking, it is possible that he or she will develop withdrawal symptoms (stressful events) that are associated with smoking abstinence. However, if social supports (such as smoking cessation groups, medical advice, etc.) are available then the individual may cope better with withdrawal symptoms than individuals without social support, eventually such that he or she can quit smoking.

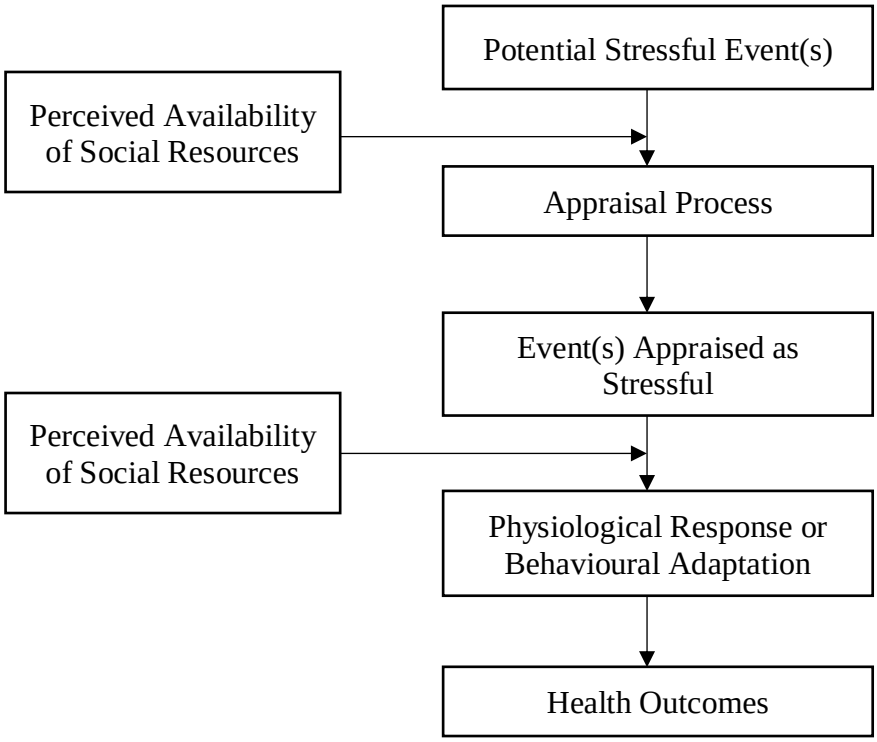


Figure 1. 3 The stress-buffering model

Adapted from Social Support Measurement and Intervention. A Guide for Health and Social Scientists. New York: Oxford University Press. Gottlieb et al., 2000

1.2 Motivation for studying loneliness

"the fear of loneliness and the desire to avoid it constitutes the ultimate primary motivational principle in man…the drive to escape isolation accounts for all our passion, thought, and action. In all we think, say, and do, we are animated by a fear of loneliness" Mijuskovic (1988)

As previous evidence suggested, deficient social relationships are linked to poor health. However, most evidence is based on studies that focused on the quantitative aspect of social relationships (e.g. the size of social network, the number of social contacts, etc.). However, individuals need more than a large social network or frequent social contacts to maintain good health and well-being. Individuals who are embedded in a larger social network, but do not form meaningful relationships with others or do not feel satisfied with social relationships are still experiencing the

deficits of social relationships and at risk of health decline. In other words, the quantity of social relationships alone is not sufficient to capture the full view of the associations between social relationships and health. In order to better understand the nature of these associations, the experience of individuals of their social connectedness should be considered. This gives rise to the motivation for studying loneliness rather than social networks alone.

1.2.1 Defining loneliness

Loneliness is a distressing feeling that is associated with deficits of social relationships, both quantitative or qualitative way (Perlman and Peplau, 1981). The definition includes three key concepts: (1) it is a subjective term that may not go hand in hand with objective social relationships (i.e. social isolation), (2) it is a negative psychological experience that differs from voluntary withdrawal from social environments, and (3) it is a deficit of social relationships whose onset can be influenced by other deficits of social relationships (Marangoni and Ickes, 1989).

1.2.1.1 Different theoretical approaches to loneliness

A wide range of scientific approaches has been developed to explain the construct of loneliness since 1970s. Broadly, the characteristics of these approaches can be categorized into three aspects: the social needs approach, the social skill approach and the cognitive approach.

The social needs approach is largely influenced by Weiss' taxonomy of two distinct types of loneliness: social loneliness and emotional loneliness. Social loneliness refers to the absence of a social network, while emotional loneliness refers to the absence of intimacy and attachments (1973). Deficits in either aspect of loneliness or both can lead to unmet social needs, which may further contribute to the experiencing of loneliness.

The social skill approach emphasizes the role of deficient social skill as the antecedent of loneliness. Social skill is the prerequisite for building and maintaining social relationships. Individuals who are experiencing loneliness are more likely to

have inadequate social skills, greater shyness and self-consciousness, as well as problems of inhibited sociability compared to those who are not lonely (Jones et al., 1982).

The cognitive approach involves the evaluation of one's obtained social relationships and desired ones. Loneliness would occur if one's obtained relationships did not match their desired ones (de Jong Gierveld, 1998). Within the cognitive approach, two conceptualizations of loneliness, unidimensional and multidimensional, have been proposed. Unidimensional conceptualisation regards loneliness as a deficit in social relationships and varies primarily in its intensity. In contrast, multidimensional conceptualization, apart from the intensity of experiencing loneliness, includes a time perspective (e.g. whether the level of loneliness changes) and emotional characteristics (e.g. abandonment, emptiness, frustration, etc.).

1.2.2 Measuring loneliness

Several measurements have been developed to assess these conceptualizations of loneliness. The most widely used unidimensional loneliness scales include single-item measurement, multi-item measurement, 3-item measurement (Hughes et al., 2004), and the revised University of California at Los Angeles (UCLA) loneliness scales (Russell, 1996). The most widely used multidimensional loneliness scales are the 11-item and the 6-item de Jong Gierveld loneliness scales (de Jong Gierveld and Tilburg, 1999; de Jong Gierveld and Tilburg, 2006). Both 11-item and 6-item de Jong Gierveld loneliness scales can be divided into social and emotional loneliness subscales following Weiss' typology, which can be used independently (de Jong Gierveld and Tilburg, 1999; de Jong Gierveld and Tilburg, 2006).

The differences between the unidimensional loneliness scale and the multidimensional loneliness scale lie in the differences in their conceptualizations. In other words, the unidimensional scales focus on the intensity of loneliness whereas the multidimensional scales can measure all three aspects (i.e. the intensity, time perspective and emotional characteristics) of loneliness. Table 1.2 presents the detailed information of each loneliness scale.

Table 1. 2 Different types of scales used to assess loneliness

- Most widely used unidimensional loneliness scale

Name	Question	Answer	Scoring method
Single-item scale	• How often do you feel lonely? OR • Do you feel lonely?	• Never, Rarely, Sometimes, Often OR • Not at all lonely, slightly lonely, lonely, very lonely	Depends on studies, either assign a score to each answer and make higher score reflect higher level of loneliness, or dichotomize answers into lonely vs. non-lonely
3-item Hughes scale (Hughes et al., 2004)	1. How often do you feel that you lack companionship? 2. How often do you feel left out? 3. How often do you feel isolated from others?	To each item: Hardly ever, some of the time, or often	Hardly ever=1 Some of the time=2 Often=3 Total score= sum of all items
Revised UCLA loneliness scale (Russell, 1996)	1. I feel in tune with the people around me. 2. I lack companionship. 3. There is no one I can turn to. 4. I do not feel alone. 5. I feel part of a group of friends. 6. I have a lot in common with the people around me. 7. I am no longer close to anyone. 8. My interests and ideas are not shared by those around me. 9. I am an outgoing person.	To each item: Never, Rarely, Sometimes, Often	Never=1 Rarely=2 Sometimes=3 Often=4 Total score= sum of all items

	10. There are people I feel close to. 11. I feel left out. 12. My social relationships are superficial. 13. No one really knows me well. 14. I feel isolated from others. 15. I can find companionship when I want it. 16. There are people who really understand me. 17. I am unhappy being so withdrawn. 18. People are around me but not with me. 19. There are people I can talk to. 20. There are people I can turn to.		

- Most widely used multidimensional loneliness scale

Name	Question	Answer	Scoring method
11-item de Jong Gierveld loneliness scale (de Jong Gierveld and Tilburg, 1999)	Emotional Subscale 1. I miss having really close friends. 2. I experience a general sense of emptiness. 3. I miss the pleasure of the company of others. 4. I find my circle of friends and acquaintances too limited. 5. I miss having people around. 6. I often feel rejected. Social Subscale 1. There is always someone I can talk to about my day-to-day problems. 2. There are plenty of people I can rely on when I have problems. 3. There are many people I can trust completely. 4. There are enough people I feel close to. 5. I can call on my friends whenever I need them.	To each item: Yes, More or less, No	Questions measuring emotional aspect are negatively worded; whereas, questions measuring social perspective are positively worded. On the negatively worded items, the neutral and positive answers are scored as '1', therefore, on question under emotional subscale, Yes=1, More or less=1, and No=0. On the positively worded items, the neutral and negative answers are scored as '1', therefore, on questions under social subscale, Yes=0, More or less=1, and No=1. The total loneliness score is the sum of score for each item. If needed, the total score can be divided into four levels: not lonely (score 0-2), moderate lonely (score 3-8), severe lonely (score 9-10), and very severe lonely (score 11).

6-item de Jong Gierveld loneliness scale (de Jong Gierveld and Tilburg, 2006)	Emotional Subscale 1. I experience a general sense of emptiness. 2. I miss having people around. 3. I often feel rejected. Social Subscale 1. There are plenty of people I can rely on when I have problems. 2. There are many people I can trust completely. 3. There are enough people I feel close to.	To each item: Yes, More or less, No	Questions measuring emotional aspect are negatively worded; whereas, questions measuring social perspective are positively worded. On the negatively worded items, the neutral and positive answers are scored as '1', therefore, on question under emotional subscale, Yes=1, More or less=1, and No=0. On the positively worded items, the neutral and negative answers are scored as '1', therefore, on questions under social subscale, Yes=0, More or less=1, and No=1. The total loneliness score is the sum of score for each item. It ranges from 0-6 with higher score reflecting greater level of loneliness.

1.2.3 Distinguishing between loneliness and social isolation

Loneliness and social isolation are two distinct concepts, though both refer to social relationship deficits. Loneliness refers to the subjective state of negative feelings towards the deficiency of social relationships, while social isolation refers to the objective state of having limited social relationships with others (Townsend and Tunstall, 1973; Wenger et al., 1996). Loneliness is by definition '*subjective'*; it is considered to be more closely associated with quality of social relationships, whereas social isolation is considered to be more closely associated with quantity of social relationships (Perlman and Peplau, 1981).

Loneliness does not always go hand in hand with social isolation. Individuals can live alone without feeling lonely, or experience loneliness in the presence of many. The relationship between loneliness and social isolation is mediated by the characteristics of the relationships and individuals' ability to optimize their social situations for themselves (i.e. limited social relationships or social resources) and adjust their expectations (Coyle and Dugan, 2012; de Jong Gierveld, 1998). For example, in a study to determine the risk factors of loneliness among rural living older people, researchers found that losing a partner is a more important risk factor for feeling lonely than having smaller social networks (Dugan and Kivett, 1994).

1.2.4 Determinants of loneliness

Loneliness can be experienced by individuals at any age (once aware of self). However, when addressing determinants of loneliness, one should bear in mind that this will vary across life stages and is largely influenced by social environments and life events.

Generally, individuals' personalities (e.g. shyness, emotional stability, agreeableness), social skills and psychosocial factors (e.g. depression, aggression, self-confidence, self-esteem) (DiTommaso et al., 2003; Vanhalst et al., 2013; Schinka et al., 2013) play important roles in determining loneliness during childhood. In young adulthood, self-esteem, the presence of a close other and the size of social network become increasingly significant (Green et al., 2001; Tritt and Duncan, 1997). In late life, the

quality of social relationships, the loss of close family members and friends, as well as the experience of physical functioning decline are all associated with greater loneliness (Pinquart and Sorensen, 2001).

1.2.5 Health consequences of loneliness

A growing body of empirical evidence indicates that loneliness is associated with greater risk of mortality (Luo et al., 2012; Patterson and Veenstra, 2010; Steptoe et al., 2013; Tilvis et al., 2011). In the most recent systematic review, after analysing data from 35 studies, researchers found that loneliness was associated with a 22% increase in all-cause mortality risk (HR: 1.22, 95% CI: 1.1, 1.4) (Rico-Uribe et al., 2018). This is consistent with the finding from an earlier systematic review that loneliness was associated with increased likelihood of mortality (Holt-Lunstad et al., 2015).

Published research also indicates that loneliness predicts morbidity, including cardiovascular risk (Caspi et al., 2006), elevated blood pressure (Hawkley et al., 2010), impaired cognitive function over time (Tilvis et al., 2004), increased risk of Alzheimer's disease (Wilson et al., 2007), depression (Cacioppo et al., 2010), sleep disturbance, deficiency and fragmentation (Harris et al., 2013; Kurina et al., 2011; Smagula et al., 2016), and physical inactivity (Hawkley et al., 2009). Moreover, the effects of loneliness on health seem to accumulate. This is well illustrated by one large study of early primary school aged children followed for 20 years (n=1037, 6 years old) in which researchers found that chronic loneliness across developmental periods (i.e. childhood, adolescence and adulthood) had a dose-response relationship to cardiovascular health risks, and the association was independent of other well-known childhood risk factors for poor adult health (Caspi et al. 2006).

1.2.6 Pathways linking loneliness to health outcomes

Several pathways through which loneliness exerts impact on health have been proposed (Hawkley and Cacioppo, 2010). Generally, these pathways can be divided into physiological and non-physiological categories.

Physiological pathway: as noted earlier, chronic loneliness in childhood predicts cardiovascular risk in adulthood in a dose-response manner (Caspi et al., 2006), which implies that the effect of loneliness on health may be rooted in physiological changes that begin in early life. Studies based on young adults suggest that loneliness is associated with increased levels of cortisol in early morning and late night, as well as the impaired immune function (Pressman et al., 2005); and during middle life, a greater salivary cortisol is found to increase during the first 30 min after awakening (Steptoe et al., 2004).

Non-physiological pathway: the effect of loneliness on health might operate through relationships with health practices (e.g. smoking, drug use) (Dyal et al., 2015; Stickley et al., 2014) and health behaviours (Hawkley et al., 2009). Previous studies report that loneliness is associated with a greater level of hopelessness during young adulthood (Page, 1991); it is linked to a decreased willingness to make efforts in maintaining and optimizing positive emotions in middle-aged adults (Hawkley et al., 2009); and it is associated with physical inactivity in later life (Newall et al., 2013).

1.3 Loneliness in older people

After examining data from the European Social Survey, Victor and her colleague found a U-shaped relationship between loneliness and age; that is, individuals aged under 25 years and those aged over 65 years are more likely to experience loneliness than those aged between 25 and 65 (Victor and Yang, 2012). This non-linear relationship between loneliness and age was also reported in a systematic review, in which researchers concluded that loneliness decreased with increasing age for individuals aged under 60 years and increased with increasing age for individuals aged over 80 years (Pinquart and Sorensen, 2001).

Unlike young or middle-aged adults, older people are at greater risk of losing family members and friends, living alone, having smaller social network size, and experiencing health decline. As a result, coping with losses and changes in health conditions become a central theme in old age. Additionally, later in life, individuals' emotions appear to be more predictable, with negative emotions becoming more infrequent than in early life. Furthermore, compared to young and middle-aged adults,

older people prefer to invest in meaningful relationships rather than building large but meaningless social connections (Charles and Carstensen, 2010). It is reported that for older people the time spent with close friends may be more enjoyable than having frequent contacts with family members (due to family responsibilities), suggesting that a good quality of social interaction is more important to older people than having frequent but less meaningful contacts (Singh and Misra, 2009).

Given the accepted fact that older people across the world consume a larger amount of health care services than their younger counterparts (World Health Organization, 2009) and given this demonstrated link between loneliness and health outcomes, loneliness itself might be related to increased demands for health services and social care. Thus, understanding the nature of loneliness in old age might not only help to prevent health consequences of loneliness but also could prevent excessive use of health resources.

1.4 Research gaps in current literature

In the current literature, evidence on loneliness in old age is mostly drawn from studies with a broad range of 'old' (aged 65 or over), meaning the oldest old (those aged 80 and over) are under-represented. There are few that focus on the oldest old. Studies of the oldest old generally are few, partly due to the challenges of researching this age group rigorously which include the fact they are more vulnerable to cognitive and physical functioning impairments, often have gatekeepers to their participation and also have a high risk of mortality (Brayne et al., 2001; Jacelon, 2007; Davies et al., 2010).

It seems likely that drawing on studies including a relatively young old age group to understand loneliness in the older old will lead to uncertainty about true applicability to this group. As stated earlier, loneliness increases with age in late life. Moreover, compared to the young-old and old-old, the oldest old have the lowest level of perceptions of good health (Chou and Chi, 2002). Furthermore, they are less likely to apply active behaviour coping strategies (i.e. efforts to deal with stressful situations, for example, whether they tried to find out more about the situation, or whether they made a plan of action and followed it) to health outcomes than young-old individuals.

This might be due to the fact that compared to the oldest old, the young-old probably still have many social resources (e.g. opportunity to obtain social support, better mobility, etc.) that could allow them to engage in active behavioural coping strategies (Martin et al., 2008).

Very few studies have investigated the relationship between loneliness and health care utilization, though one systematic review examining the relationship between social relationships and health care usage in high income countries has been published (Valtorta et al., 2018).

1.5 Aims and research questions

The aim of this thesis is to investigate loneliness in the oldest old, to test and estimate how loneliness is related to poor health-related outcomes, and to assess how it influences health service usage.

Specific objectives are:

(1) To investigate the determinants of loneliness in the oldest old.
(2) To explore changing patterns of loneliness in the oldest old over time.
(3) To examine risk factors that predict changes in loneliness over time.
(4) To investigate the association between loneliness and health-related outcomes, e.g. the impact of loneliness on all-cause mortality and cognitive function decline.
(5) To conduct a narrative review of the literature and synthesize evidence related to the impact of loneliness on health service use in order to refine specific questions to be addressed through primary analysis.
(6) To investigate whether feeling lonely increases the demands for healthcare services.

This thesis is based on data from the Cambridge City over-75s Cohort (CC75C) study. CC75C is a population-based prospective cohort study of the very old, which began in 1985 and included 2166 men and women aged at least 75 years old. The detailed information about this dataset will be described in Chapter 3.

Apart from research aims and objectives mentioned above, a qualitative study exploring the conceptualisation of loneliness in different cultural contexts (i.e. UK and China) is also conducted. The rationale of conducting the qualitative study is that there has been no consistent definition of loneliness, the conceptualisation of loneliness in empirical analyses is exclusively from researchers' point of view. However, one of the scientific research goals is to generate knowledge that has practical relevance to lived lives, exploring what people mean when they are asked to define loneliness is vital to understand loneliness fully, including how this concept might very across cultural contexts. Since the respondents of the qualitative study are not limited to the oldest old, findings from this study are reported in Appendix S.

1.6 Thesis structure

Based on research aims, the thesis includes nine chapters as shown below in Figure 1.4.

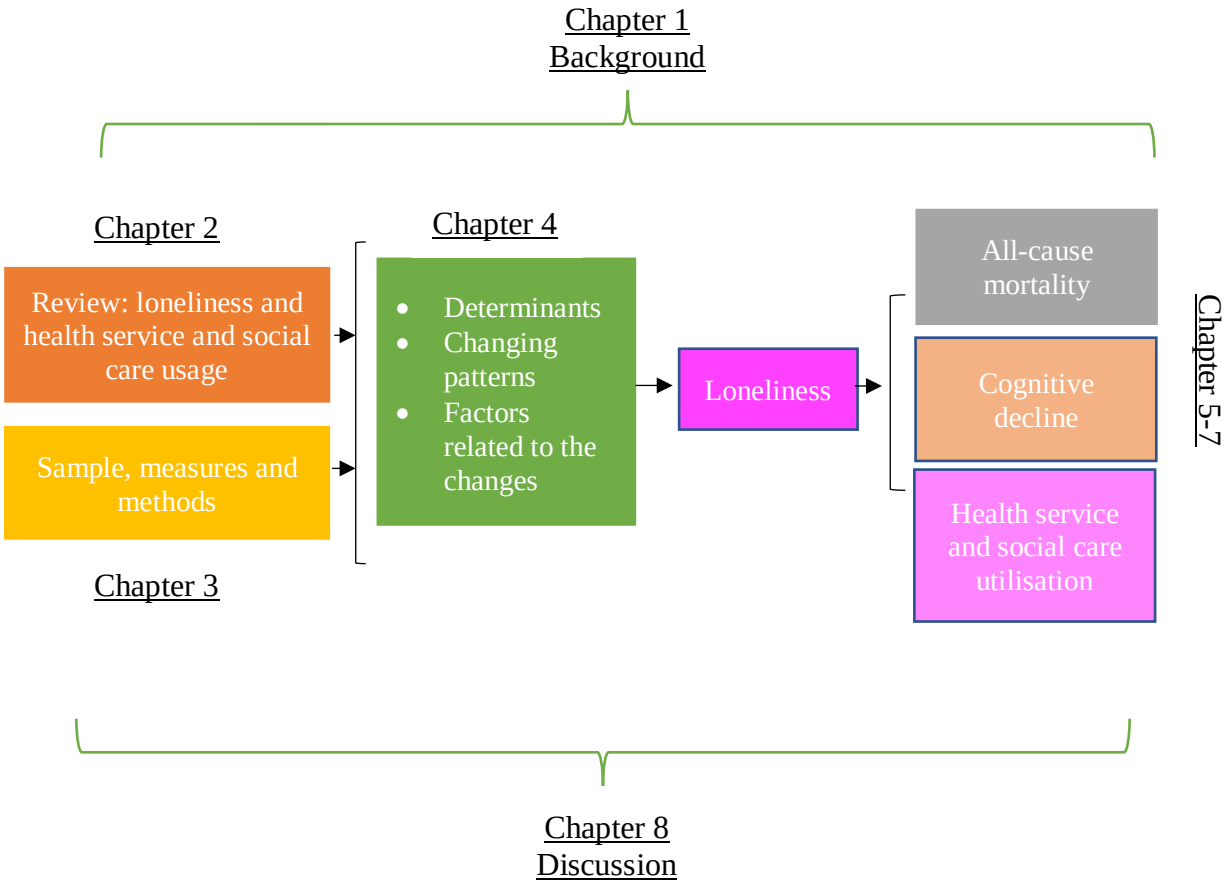
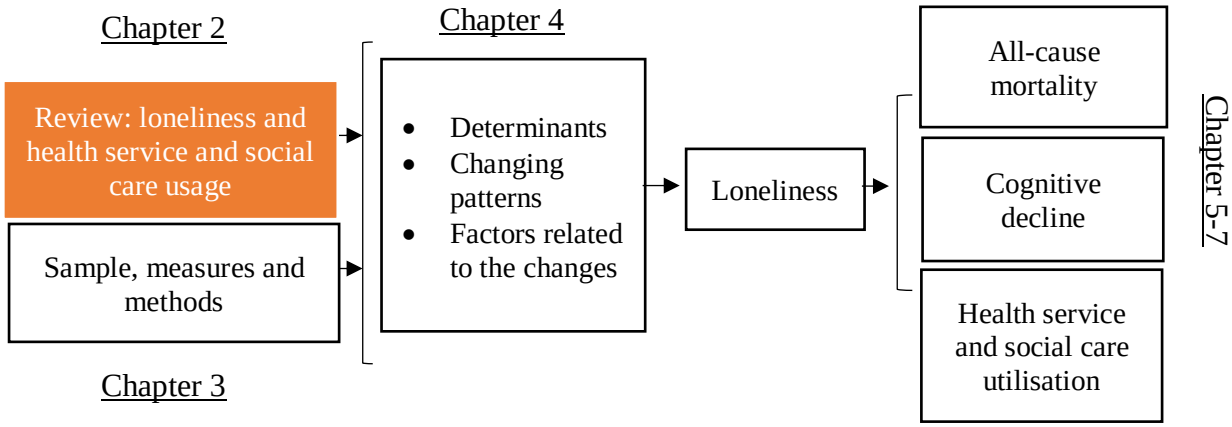


Figure 1. 4 Thesis structure

Chapter 2 Review and Evidence Synthesis: Loneliness and Health Service and Social Care Utilization

2.1 Chapter Overview

This chapter aims to understand prior knowledge and identify research gaps in the existing studies on the association between loneliness and health service and social care usage.



2.2 Systematic Review

2.2.1 Introduction

Loneliness is a common phenomenon across ages. There is a U shaped relationship of loneliness with age, demonstrated in the UK and countries across the western worlds (Nicolaisen and Thorsen, 2014; Victor and Yang, 2012). According to a literature review, just under half of those in early adulthood express loneliness (44%), around a fifth to a third in mid-life and a quarter in the younger old, and four out of 10 in the older old (Dykstra, 2009).

Given the relationship described in earlier chapter of loneliness with a range of poor health outcomes, it is plausible to hypothesise that loneliness may indirectly increase the demands for health care services. Furthermore, recent studies have reported that loneliness itself might be associated with frequency of use of health services (Ellaway et al., 1999). However, findings about loneliness and healthcare service usage from current evidence are inconsistent; some studies found a significant association between loneliness and care service (Andren and Rosenqvist, 1985; Cheng, 1992; Geller, 2004), while others found no association (Bock et al., 2017; Burr and Lee, 2013). Owing to the various domains of health services studied, and the differences in study design, population and methodologies, it is difficult to have a general view on the association between loneliness and care services use.

A systematic review is useful for synthesizing the existing evidence and clarifying the consistency of findings. No reviews on the independent effect of loneliness on health service and social care usage have been published to date, with the exception of one systematic review focusing on the association between social relationships and health care utilization in older adults. In this review social relationships were assessed through the structure of social network, the availability of social support and individual's perceived social support (Valtorta et al., 2018). Although this thesis as a whole focuses on loneliness in the oldest old, given the high prevalence of loneliness in young and old populations and its adverse consequences on health, the rising demand for healthcare services (World Health Organization, 2009), as well as the lack of evidence on loneliness and healthcare services use in the oldest old population, this

review will focus on loneliness as a risk factor for social and health service usage from a life course perspective. The specific objective of this chapter is therefore to review published evidence on the association between loneliness and health service and social care usage in population, regardless of age.

2.2.2 Methods

2.2.2.1 Search strategy

Four databases were used to gather evidence, which were PubMed, Embase, Scopus and PsycINFO. Search terms for loneliness were *"loneliness" OR "lonely" OR "feel alone" OR "feel isolated" OR "subjective isolation" OR "emotional lonely",* and for social/health service were *"social service" OR "health service" OR "general practice" OR "physician visit" OR "hospital* admission" OR "emergency department" OR "informal care" OR "formal care" OR "day care" OR "community service use".* The use of wildcat operator, i.e. "*", was intended to capture as many of the permutations of the phrase as possible. Furthermore, where it was possible, exclusion criteria such as non-human, language other than English and review articles were applied in a given database. In addition, reference checking from identified articles was also included. Reference searching was originally conducted in June 2017 and then updated in November 2017. All articles published before 6th November 2017 were eligible for inclusion.

2.2.2.2 Study selection

To be included in this review, studies had to have (1) loneliness as the primary exposure and (2) social or health service use as the primary outcome. Studies that were qualitative studies, reviews, conference proceedings, book chapters, and not written in English were not included. Title and abstract screening were conducted by three independent reviewers (HW, SW and ZY) based on inclusion and exclusion criteria. Full-text screening was carried out independently by two reviewers (HW and SW). Differences in title, abstract and full-text screening were resolved through discussion.

When full-text of eligible articles could not be located, the first author, the principal investigator of the dataset used in that specific study, as well as published journals, were contacted. This review was reported following the statement by Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) (Moher et al., 2010). Detailed information of the literature search is shown in Figure 2.1.

2.2.2.3 Data extraction

Data extraction was conducted by two reviewers (HW and SW) separately. A standard Microsoft Excel spreadsheet was used to store extracted information including author(s), published year, study setting, study design, characteristic of participants, assessment of loneliness, prevalence of loneliness, measure of social or health service use, controlled covariates and study results. The description of each study is provided in Table 2.5 (at the end of this chapter).

2.2.2.4 Quality assessment and evidence strength synthesis

The quality of individual studies was assessed by the two reviewers using the Newcastle-Ottawa Scale (NOS) (Wells et al., 2012), and any disagreements were resolved by discussion. Because of the heterogeneity of studies, a meta-analysis could not be conducted. To summarize findings and to present them incorporating their qualities, an algorithm for grading the strength of evidence developed by Gomes and Higginson (2006) was adapted (Figure 2.2). Strong and moderate evidence was described in detail in the results section, while weak evidence was described only when they had different outcome domains measured apart from those in strong and moderate strength studies.

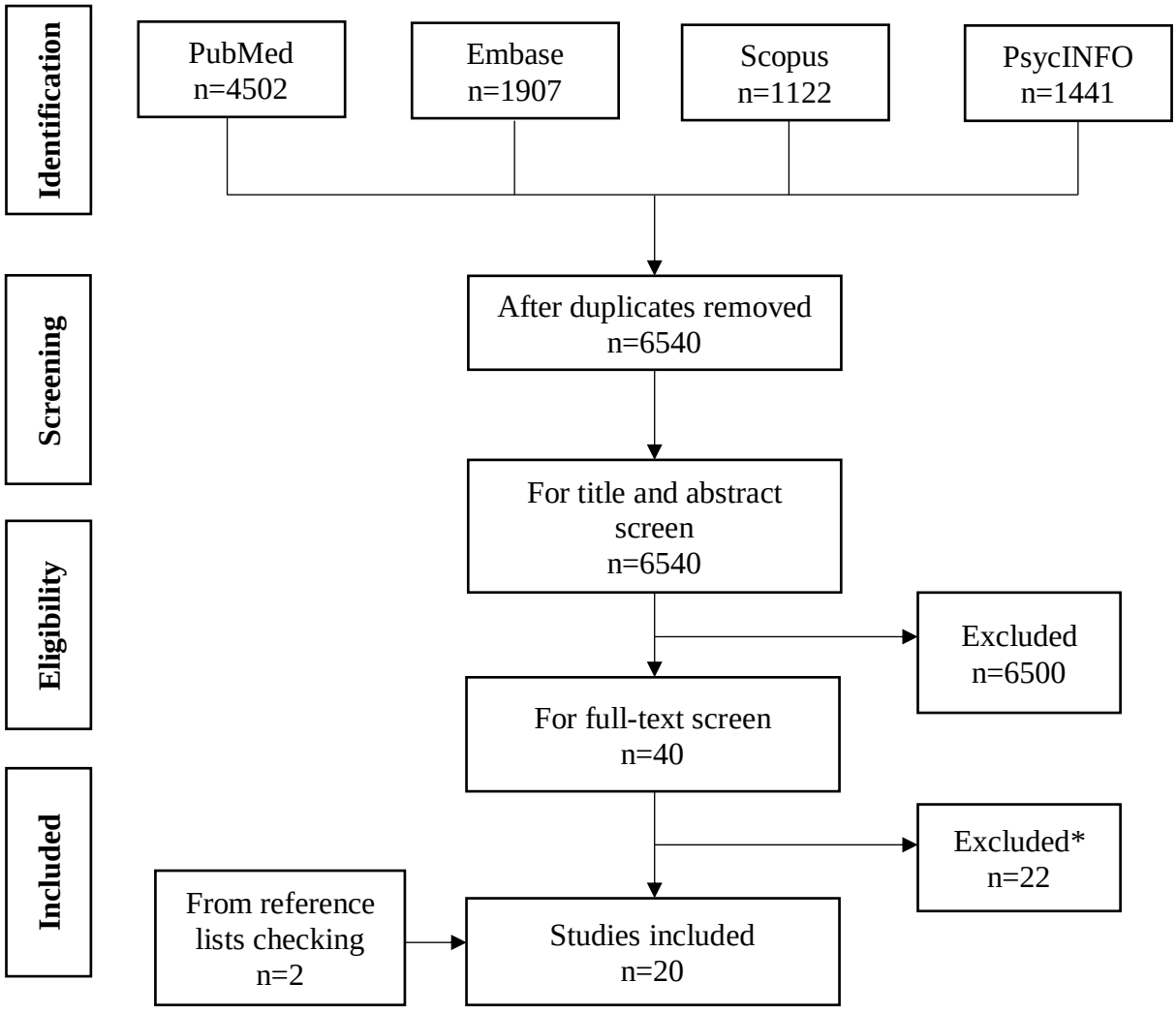


Figure 2. 1 Flowchart of literature search and selection

Note: *: one study could not be allocated through the contact with the author, the principal investigator of database manager or published journal.

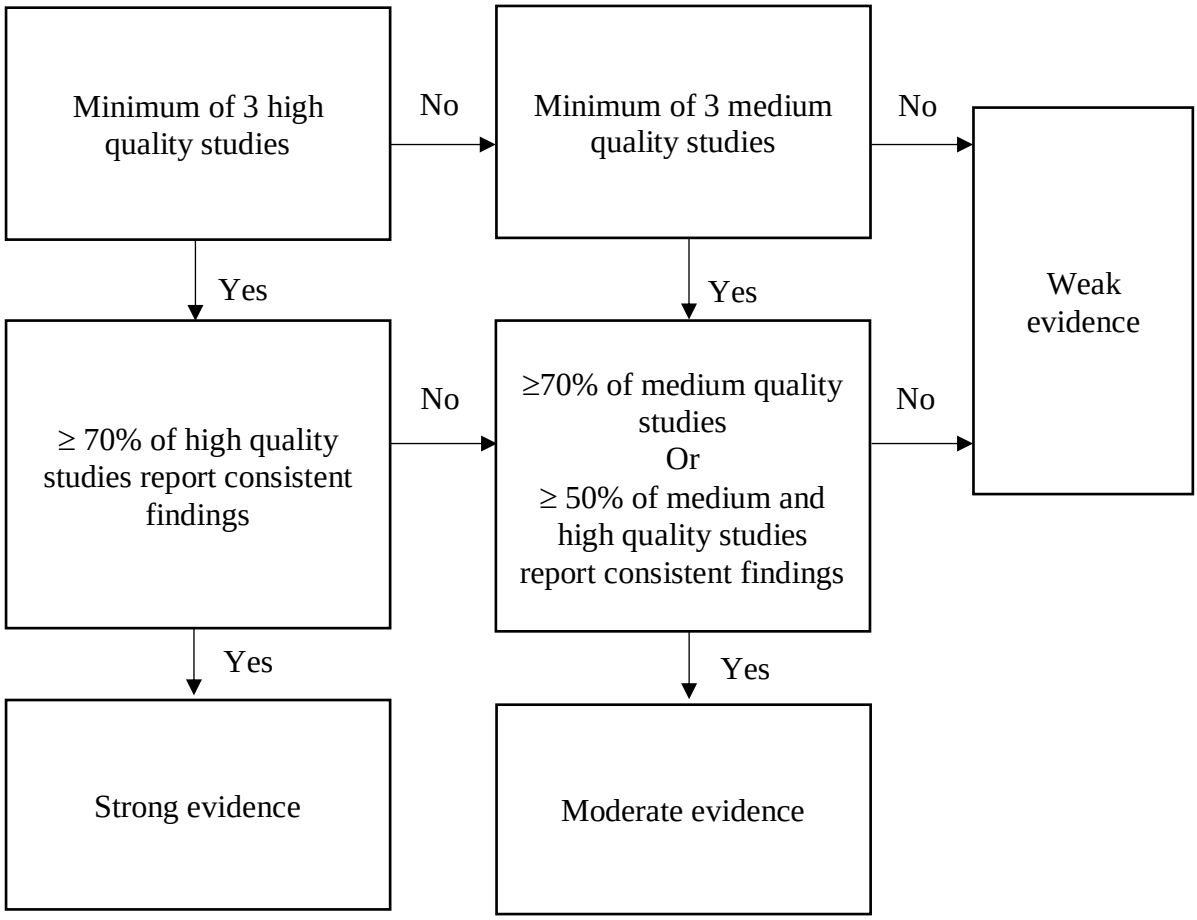


Figure 2. 2 Flowchart of quality appraisal process

Note: Algorithm adapted from Gomes and Higginson, 2006. High quality was defined if the study had score ≥7 on NOS scale and had performed multiple regression analyses, medium quality was defined if the study had score <7 on NOS scale but had performed multiple regression analyses or the study had score ≥6 on NOS scale but without multiple regression analyses, and low quality was defined if the study had score <6 and did not have multiple regression analyses.

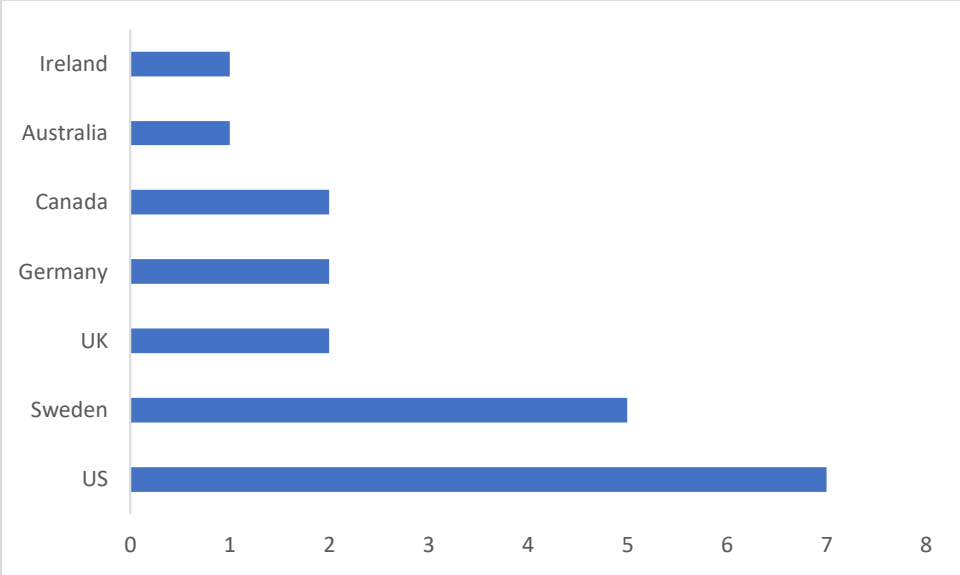


Figure 2. 3 Number of studies by country

2.2.3 Results

After removing duplicates, 6540 articles were identified. 6500 of these were excluded after title and abstract screening, leaving 40 articles for full-text assessment. 22 articles of these were excluded according to pre-defined inclusion and exclusion criteria, and an additional 2 articles were allocated through 'snow-balling' i.e. reference checking of identified articles (Figure 2.1).

The studies were primarily conducted in the US (n=7) and Sweden (n=5), covering over 36,000 participants aged 14 years and over (Figure 2.3). Most reported studies have focused on older people, a total of 11 out of 20 studies were exclusively based on older people (i.e. aged 60 or over) (Table 2.4, 2.5). Most were cross-sectional (n=13), followed by longitudinal (n=6) with one case-control study. Most were population-based (n=13), the rest were hospital-based including participants who were either frequent users of hospital emergency department or primary care practices, and patients with chronic heart failure (Table 2.1, 2.5). The association between loneliness and health service use was examined in almost all studies (n=19), with only one study particularly investigating the association between loneliness and social service use.

Table 2. 1 Summary of studies by study design and setting

Study design	Study setting		Total
	Hospital-based	Community-based	
Cross-sectional	5	8	13
Longitudinal	1	5	6
Case-control	1	-	1
Total	7	13	20

There was a great heterogeneity in the methods used to capture loneliness, from single-item scales (n=7) to the 3-item Loneliness Scale developed by Hughes (n=4), multiple-item scale (n=1), two versions (i.e. the 6-item and the 11-item) of de Jong Gierveld Loneliness Scales (n=2), and three versions (the version 3, the 4-item and the 10-item) of UCLA Loneliness Scales (n=4). For studies that assessed loneliness by using single-item scales, the scales differed between studies (Table 2.5).

Most studies (n=13) reported the prevalence of loneliness ranging from 2% to 60%; a few (n=6) reported a mean loneliness score, and one did not provide either prevalence or mean score of loneliness (Table 2.5).

Health service use was measured for seven different domains: hospital admission, outpatient visits (e.g. physician visits, general practice (GP) visits, primary care visits, specialists visits), emergency department visits, hospital re-admission, length of hospital stay, dental care service use and health expenditure. Social service use was assessed by either asking participants whether they need and have used domestic help for daily or weekly living tasks or measuring the frequency of nursing home admission. A summary of health and social services is listed in Table 2.2.

Table 2. 2 Summary of health service and social care domains

Health care service	Number of studied articles (n)	Social care service	Number of studied articles (n)
Hospital admission	5	Domestic help	1
Hospital re-admission	3	Nursing home admission	1
Length of hospital stay	4		
Outpatient visit	11		
Emergency department visit	4		
Dental care service	1		
Health expenditure	1		

2.2.3.1 Health service use

The associations between loneliness and health service use were reported by strength of evidence, the strong evidence was reported firstly, followed by moderate and weak (summary in Table 2.3). In addition, evidence based on the oldest old was found to be limited in the published literature. To have a general sense of the relationship between loneliness and healthcare service utilisation in older people, findings from studies that were based on older population (here referred to individuals who were aged 60 years or older) were summarized (Table 2.4).

Table 2. 3 The association between loneliness and health service and social care usage by strength level

	Strong evidence		Moderate evidence		Weak evidence
	Association	**Consistency**	**Association**	**Consistency**	**Association**
Health services					
Hospital admission	No effect	100% (4/4)			
Outpatient (GP, specialist, physician, hospital) visits	No effect	70% (2/3)			
Emergency department visits			+	100% (4/4)	
Hospital re-admission					Mixed
Length of hospital stay					Mixed
Dental care service use					No effect
Monthly health care spending					-
Monthly inpatient health care spending					-
Monthly outpatient health care spending					No effect
Monthly SNF spending					No effect
Social services					
Social services (help for daily or weekly living)					+
Nursing home admission					+

Note: '+' indicates positive association; '-' indicates negative association; GP: general practice; SNF: skilled nursing facility

2.2.3.1.1 Hospital admission

The impact of loneliness on hospital admission was investigated in four high quality studies (Bock et al., 2017; Gerst-Emerson and Jayawardhana, 2015; Molloy et al., 2010; Newall et al., 2015), and one medium quality study (Geller et al., 1999). Participants in all high quality studies were community-based, while participants in the medium quality study were emergency department health service users. However, regardless of study quality, no study found a significant association between loneliness and hospitalisation.

2.2.3.1.2 Outpatient visits

Eleven studies (Berg et al., 1981; Beutel et al., 2017; Bock et al., 2017; Cheng, 1992; Ellaway et al. 1999; Geller, 2004; Gerst-Emerson and Jayawardhana, 2015; Hand et al., 2014; Lauder et al., 2004; Newall et al., 2015; Taube et al., 2015) tested the influence of loneliness on the frequency of outpatient visits, of which 3 were of high quality (Bock et al., 2017; Gerst-Emerson and Jayawardhana, 2015; Newall et al., 2015), 5 were of medium quality (Ellaway et al. 1999; Cheng, 1992; Geller, 2004; Hand et al., 2014; Lauder et al., 2004) and 3 were of low quality (Berg et al., 1981; Beutel et al., 2017; Taube et al., 2015). 2 out of 3 high quality studies (Bock et al., 2017; Newall et al., 2015) and 2 out of 5 medium quality studies (Hand et al., 2014; Lauder et al., 2004) found no evidence of an association between loneliness and frequency of outpatient visits, while the remaining studies reported mixed findings. For example, 1 medium quality study (Cheng, 1992) found strong association between loneliness and general practice visits or primary care visits, one medium quality study (Ellaway et al., 1999) reported that loneliness was associated with general practice consultation at surgery, but not at home, and another medium quality study (Geller, 2004) reported that loneliness was significantly associated with unscheduled hospital visits by pregnant women.

2.2.3.1.3 Emergency department visits

Four studies (Andren and Rosenqvist, 1985; Andren and Rosenqvist, 1987; Geller et al., 1999; Molloy et al., 2010) examined the association between loneliness and the

frequency of emergency department visits. One was of high quality (Molloy et al., 2010) and the other three were of medium quality. All studies found a significant association between loneliness and emergency department visits regardless of study settings (i.e. the high quality study focused on community-based individuals, whereas participants in all three medium quality studies were emergency department users). However, only the high quality study accounted for potentially important confounders, such as participants' health status.

2.2.3.1.4 Hospital re-admission

Evidence for the association between loneliness and hospital re-admission was examined in one high quality study (Newall et al., 2015) and one medium quality study (Hawker and Romero-Ortuno, 2016). Evidence from the high quality study showed that loneliness predicted re-hospitalisation over a 2.5-year follow-up after controlling for self-rated health and chronic health conditions, whereas evidence from the medium quality study did not find such association within a 30-day period.

2.2.3.1.5 Length of hospital stay

Of four studies (Hawker and Romero-Ortuno, 2016; Lofvenmark et al., 2009; Newall et al., 2015; Taube et al., 2015) examining the association between loneliness and length of hospital stay, one was of high quality (Newall et al., 2015), one was of medium quality (Hawker and Romero-Ortuno, 2016) and two were of low quality (Lofvenmark et al., 2009; Taube et al., 2015). Evidence from these studies was mixed, with some studies (Newall et al., 2015; Taube et al., 2015) reporting no association between loneliness and length of hospital stay, but others (Hawker and Romero-Ortuno, 2016; Lofvenmark et al., 2009), including one study of patients with coronary heart disease (Lofvenmark et al., 2009), reporting significant associations.

2.2.3.1.6 Dental care service use

The association between loneliness and dental care service utilization was examined in one study (Burr and Lee, 2013) by using data from a Health and Retirement Study, and researchers did not find significant association between loneliness and use of

dental services after controlling for socio-demographic characteristics and health status.

2.2.3.1.7 Health-related cost

By linking data from US subjects representative of the older population aged 50 or over and the Medicare beneficiary summary files, one study (Shaw et al., 2017) looked at the association between loneliness and Medicare spending over a 4-year follow-up, and reported loneliness was negatively associated with total monthly Medicare spending after adjusting for socio-demographic characteristics, financial status and health status. In particular, loneliness predicted lower monthly inpatient spending, monthly outpatient spending and monthly skilled nursing facility spending. All associations, except the association with monthly inpatient spending, were not significant.

2.2.3.2 Social care service use

2.2.3.2.1 Domestic help service use

The study (Berg et al., 1981) that examined the association between loneliness and domestic help service usage was of low quality. Results from this study showed that there were no differences in demands for personal help between lonely and non-lonely individuals, but lonely women expressed more need for domestic help and they used more social services for helping with daily or weekly home tasks than those not expressing loneliness.

2.2.3.2.2 Nursing home admission

One study (Russell et al., 1997) examined the effect of loneliness on subsequent nursing home admission over a 4-year follow-up among rural elders (aged 65 or over) and found that only severe loneliness significantly predicted nursing home admission after adjusting for socio-demographic characteristics, financial status and health. No such associations were found among individuals who had other levels of loneliness.

2.2.3.3 Health and social care usage in older people

In general, findings from studies that were exclusively based on older people were consistent with the overall conclusions except for outpatient visits and hospital re-admission. Regarding outpatient visits, the overall finding indicated that there was no significant relationship between loneliness and outpatient visits. Studies focused on older people reported mixed findings. For hospital re-admissions, findings from one high quality study and one medium quality study suggested mixed findings. The study based on older people (medium quality) reported no association between loneliness and hospital re-admission.

Similarly, findings from older samples were generally consistent with findings from mixed young and old or young only populations with the exception of hospital re-admission. In the study with a mixed young and old sample (age range: 45-95 years), researchers found that lonely individuals had higher odds of being re-hospitalised than their non-lonely counterparts (OR=1.74, 95%CI: 1.01-3.00) after controlling for a series of health problems (Newall et al., 2015). In contrast, the study based on older people (mean: 85.1 years, SD: 5.8) did not find such an association (Hawker and Romero-Ortuno, 2016).

Table 2. 4 The association between loneliness and health service and social care usage in older people

Outcome domain	Overall conclusion	Conclusion of studies with young sample or a mixed young and old population	Conclusion of studies with older population	Studies*
Hospital admission	No effect (n=5)	No effect (n=3)	No effect (n=2)	Gerst-Emerson & Jayawardhana, 2015; Molloy et al., 2010
Outpatient visits	No effect (n=11)	No effect (n=5)	Mixed (n=6)	Berg et al., 1981; Cheng, 1992; Ellaway et al., 1999; Gerst-Emerson & Jayawardhana, 2015; Hand et al., 2004; Taube et al., 2015
Emergency department visits	+ (n=4)	+ (n=3)	+ (n=1)	Molloy et al., 2010
Hospital re-admission	Mixed (n=2)	+ (n=1)	No effect (n=1)	Hawker & Romero-Ortuno, 2016
Length of hospital stay	Mixed (n=4)	No effect (n=1)	Mixed (n=3)	Hawker & Romero-Ortuno, 2016 ; Lofvenmark et al., 2009; Taube et al., 2015
Dental care service use	No effect (n=1)	NA	No effect (n=1)	Burr & Lee, 2013
Health-related cost	Mixed (n=1)	Mixed (n=1)	NA	
Social services (help for daily or weekly living)	+ (n=1)	NA	+ (n=1)	Berg et al., 1981
Nursing home admission	+ (n=1)	NA	+ (n=1)	Russell et al., 1997

Note: '*' indicates the studies with older people; 'n=' indicates the total number of studies on specific outcome domain or the total number of studies on specific outcome domain in older population; NA: not applicable; green: findings of studies based on older people was consistent with overall finding based on strength of studies on same outcome domain; orange: findings of studies based on older people was not consistent with overall finding based on strength of studies on that specific outcome domain.

2.2.4 Discussion

2.2.4.1 Main findings

In this review, strong evidence was found that loneliness was not independently associated with frequency of hospital admission or outpatient visits. In contrast, there is moderate evidence suggesting a significant association between loneliness and emergency department use. There appeared to be a gender effect with women expressing loneliness reporting more use of social services for domestic tasks than those who did not. Loneliness is associated in older people with transitions to care settings.

2.2.4.2 Strengths and limitations of the review and of the literature itself

This is the first systematic review to synthesize evidence on loneliness and health service and social care usage in individuals across all age groups. Different settings across the care system were included. Careful consideration has been given to the selection of tools, appraising for quality.

However, a considerable heterogeneity was found in study populations, designs and measurements. The most used measurement was a single-item scale developed by researchers and they varied in different studies. For example, in one study, participants were asked whether they feel lonely, while in another study, participants were asked whether they are alone or have few contacts; the latter measurement was more like an assessment for social isolation rather than for loneliness. Furthermore, confounders adjusted for in each study varied, and many studies did not take potentially important confounders, such as health conditions, into consideration. Despite the fact that an age restriction was not applied in the literature search, most published studies focused on older people. Findings that were exclusively based on older population were summarized separately and compared with the overall findings, as well as findings from studies with young only, or mixed young and old samples. On the other hand, those studies with a mixture of young and older people did not include subgroup analyses. Therefore, it was not possible to distinguish the effects of

loneliness on health service use in different age groups in these specific studies. As stated in Chapter 1, the determinants for loneliness are different between young and old people (de Jong Gierveld, 1998), so it is likely that the pathways through which loneliness exerts effects on health service use are different. Most studies dichotomized the answers to lonely questions for ease of statistical analysis, but this approach limits the ability to examine the severity of loneliness and service use. Additionally, most were cross-sectional studies, and reverse causality is possible, if not probable. Individuals who used health services more frequently may be more likely to feel lonely for a variety of reasons including disruption of their social engagement patterns.

2.2.4.3 Interpretation of findings

The findings reveal a complicated relationship between loneliness and health service use. This is partly due to the different types of health service examined in included studies, and also because of the heterogeneity of study populations. For example, according to studies involving community-dwelling participants, loneliness was not related to outpatient healthcare service use. However, in the case-control study that aimed to study loneliness in pregnant women compared to a non-pregnant control group, researchers found that loneliness was strongly related to unscheduled hospital visits in pregnant women. They also found that the combination of younger age and loneliness predicted the highest hospital service usage. One possible explanation put forward is that lonely pregnant women, especially the younger ones, may have fewer resources to obtain pregnancy-related information than non-lonely pregnant women. Hospitals might be serving as a secure base for these women at a time of uncertainty.

Despite the fact that all those studies that examined the influence of loneliness on emergency department visits reported a significant association, findings from 3 out of 5 studies were based on participants who were frequent emergency department users, implying that the participants were already in need of health-related services. Moreover, these studies did not adjust for participants' health status. Illustrating the importance of looking at potential mediating factors is a national study from the US based on older community-dwellings, this study found a relationship between emergency room attendance and poor self-rated health as well as chronic disease

(Morris et al, 2014). Thus, rather than indicating a significant association between loneliness and emergency department use, the findings of this review would suggest that more studies are required to test whether the association is independent of the interaction between loneliness and health conditions.

No significant associations between loneliness and hospital admission were found. This finding was based on high quality studies that were adjusted for health conditions, health behaviours and psychological factors such as depression or stress. There was also no significant relationship between loneliness and dental care service use. Surprisingly, an unexpected result was found that loneliness predicted decreased health expenditure, while mixed findings were reported on the association between loneliness, hospital re-admission and length of hospital stay. Overall, the findings from this review do not indicate that loneliness is a significant risk factor for health service use when appropriate confounders are taken into account. This is consistent with the findings of a systematic review looking into the relationship between social relationships and health service usage in which researchers concluded that, independent of health conditions, social relationships were not related to increased health service demand (Valtorta et al., 2018).

Only two studies have explored the relationship between loneliness and social service use, only one of which tested effect sizes. Further research is needed on this topic.

The lack of evidence for the association between loneliness and most health service domains may suggest that lonely individuals are less likely to take active coping strategies (Valtorta et al., 2018). This is indirectly supported by the finding of Dimatteo (2004) that the level of patients' adherence to medical treatment is influenced by their social networks, that is, the stronger level of social support, the greater level of adherence to treatment. Another possible explanation could be that loneliness is associated with higher risk of morbidity and mortality (Chapter 1), indicating that lonely individuals are unhealthier than their counterparts and seek less care when more would be ok. Individuals who lack social support or have smaller social networks but are high users of health-related services may be more likely to be advised to go into nursing homes (Steinbach, 1992). The significant and mixed findings for the association between loneliness and other health services, such as

emergency department use or hospital re-admission, suggests different pathways. However, most of the evidence in the review was from studies with medium or low quality, which meant that they were either lacking proper statistical analysis to test the effect size or analysis did not adjust for important confounders, such as health conditions. Therefore, to better understand the nature of loneliness and health service use, it is critical for future research to take health conditions into account.

2.3 Conclusion

In summary, this systematic review suggests that lonely individuals do not have greater use of many types of health and social care services. No consistent differences were found between older people and general population in these analyses. This challenges the widely accepted public notion that loneliness is associated with increased consumption of healthcare resources. On the other hand, given the high prevalence of loneliness experienced by people across ages, the close relationship between loneliness and nursing home admission as well as between loneliness and domestic service use, identifying individuals who are at greater risk of feeling lonely and implementing interventions aimed at improving the quality of social relationships might help with reduction of social care service consumption. Future researchers need to focus on developing a strategy about how to measure loneliness more consistently in order to reduce the considerable heterogeneity of assessment to date. This also might be of benefit for intervening in the development of loneliness and the prevention of unnecessary consumption of health and social care services.

This thesis focuses on loneliness in the oldest old. At present, because of limited evidence on the association between loneliness and health service and social care utilisation stratified by age, it is not clear whether loneliness increases the demand for health service and social care for individuals who are in the oldest old age group. Moreover, to support "ageing in place" (defined as remaining in the community rather than in residential care (Wiles et al., 2012)) and avoid unnecessary costly institutional care, research focusing on examining the association between loneliness and community service utilisation is needed. These questions are addressed in Chapter 7 through longitudinal analyses of repeated measures of loneliness and community health service utilisations in the oldest old. Before this, descriptions of dataset,

measures and statistical methods that will be used in Chapter 7 and other subsequent chapters will be reported in next chapter.

Table 2. 5 Description of studies included in the systematic review

Study	Setting	Design	Participants (n, % male)	Age	Loneliness Measure	% loneliness	Health/Social service measure	Covariates	Results	Quality
Andren and Rosenqvist, 1985[#]	Sweden, Hospital	Cross-sectional	232 % male not reported	≥16	Not reported	26.5%	Frequency of ED visits	Age Sex	OR=3.23[*]	5
Andren and Rosenqvist, 1987[#]	Sweden, Hospital	Longitudinal two-year follow-up	232 Male vs. Female ratio 1.17	Median age range: 50-54 at baseline	Not reported	32.0%	Frequency of ED visits	Not reported	RR=2.70[*]	4
Berg et al., 1981	Sweden, Community	Cross-sectional	1007 47% male	All 70 years old	Single-item "Do you feel lonely" "often" or "sometimes" coded as positive "rarely" or "never" coded as negative	12.2% sometimes lonely 6.5% often lonely	Medical usages (i.e. medical advice) Social service (i.e. daily/weekly domestic help service)	Not reported	34% lonely vs. 21% non-lonely females for medical usage Effect size not reported, but lonely females reported greater demands on social services	5
Beutel et al., 2017	Germany, The Gutenberg Health	Cross-sectional	14661 51% male	Mean (SD): 54.9 (11.1) (age	Single-item "Are you alone / do you have few contacts?"	4.9% slightly lonely	Frequency of physician visits in preceding month	Not reported	63% lonely vs. 42% non-lonely individuals for	5

	Study (GHS)			range: 35-74)	(No=0, Yes but I don't suffer=1, Yes and I suffer slightly=2, Yes and I suffer moderately=3, suffer strongly=4)	3.9% moderate lonely 1.7% severely lonely	Frequency of inpatient treatments in preceding 12 months		≥ 1 physician visit 21% lonely vs. 13% non-lonely individuals for ≥ inpatient treatment	
Bock et al., 2017	Germany, The 2-4 waves of the German Ageing Survey (DEAS)	Longitudinal three follow-ups (2002, 2008 and 2011)	Number of participants and % of male were not reported, but there were total 7116 observations	≥40 at baseline	A short version of 11-item (6-item) de Jong Gierveld Loneliness Scale	Mean (SD): 1.7 (0.5) (score range: 0-6)	Frequency of outpatient (GP/specialist) visit Hospital admissions	Age SES[1] HC[1] HB[1]	GP visits: β=-0.038 Specialist visits: β=0.005 Hospital admission: OR=1.066 (95% CI: 0.842-1.351)	7
Burr and Lee, 2013	US, 2008 Health and Retirement Study (HRS)	Cross-sectional	2978 44% male	Mean: 74.2 (age range: 65+)	Index based on responses (often=3, sometimes=2, never=1) to how often do you feel:	Mean: 1.6 (score range: 1-3)	Frequency of dentist visits in the preceding 2 years	Age Sex Race SES[2] HC[2] PF[1] SF[1]	OR=1.181 (95% CI: 0.893-1.562)	6

					Lack companionship Left out Isolated In tune with those around you Alone					
Cheng, 1992	US, Community	Cross-sectional	Sample A: 112 females Sample B: 115 females	Mean: 73 (age range: 65-85)	A 10-item UCLA Loneliness Scale	Not reported	Frequency of physician visits	HC[3] PF[2]	From sample A: β=0.27[**] From sample B: β=0.31[**]	6
Ellaway et al., 1999	UK, Community	Cross-sectional	691 45% male	318 aged 40 years 373 aged 60 years	Single-item "Loneliness can be a serious problem for some people and not for others. At the present moment do you ever feel lonely?" Most of the time/quite often = 3 Occasionally=2 Seldom/never=1	5.1% most of the time/often lonely 15.1% occasion-ally lonely	Frequency of GP visits at surgery during the past year Frequency of GP visits at participants' home during the past year	Age Sex SES[3] HC[4]	Mean of GP visits at surgery according to loneliness levels[**]: 7.8 for most of the time/often lonely, 3.4 for occasionally lonely and 4.2 for seldom/ never lonely Mean of GP visits at home: 0.57 for most	7

									of the time/often lonely, 0.21 for occasionally lonely and 0.39 for seldom/ never lonely	
Geller et al., 1999	US, Hospital	Cross-sectional	164 ED users 42% male	≥14	Version 3 of the UCLA Loneliness Scale	Mean (SD): 39.1 (12) (score range: 20-80)	Number of hospital visits (including ED visits and direct hospital visits) Hospital admission	Not reported	Total hospital visits: $\beta=0.063^{***}$ Hospital admission: effect size not given, but reported that the association was not significant	5
Geller, 2004	US, Hospital	Case-control	Case group: 53 consecutive pregnant women in first trimester Control group: 61 non-	Case group: mean 22.4 Control group: mean 25.7	Version 3 of the UCLA Loneliness Scale	Case group: mean 41.0 Control group: mean 43.0 Score range 20-80	Number of pregnancy-related unscheduled hospital visits	Age	$\beta=0.076^{*}$	6

			pregnant women							
Gerst-Emerson and Jayawardhana, 2015	US, 2008 and 2012 the Health and Retirement Study (HRS)	Longitudinal four-year follow-up	3530 % male not reported	Mean: 71 (age range 60-100) in 2008	3-items loneliness scale Primary loneliness: a response of "some of the time" or "often" to any of the 3 scale measures Alternative loneliness: a response of "some of the time" or "often" to at least 2 of the 3 scales	Year 2008: Primary loneliness: 52.7% Alternative loneliness: 35.0% Year 2012: Primary loneliness: 56.6% Alternative loneliness: 37.1%	Number of physician visits Hospital admission	Age Sex Race SES[4] HC[5] PF[3]	Physician visits: primary loneliness in both years: β=0.075*, alternative loneliness in both years: β=0.073* Hospital admission: primary loneliness in both years: β=0.048, alternative loneliness in both years: β=0.059	7
Hand et al., 2014	Canada, Primary care practice	Cross-sectional	40 45% males	Mean (SD): 81.3 (5.9)	3-items loneliness scale	Mean (SD): 4.1 (1.3) (score range 3-7)	Number of primary care visits in previous year	HC[6]	β=-0.16	4
Hawker and Romero-Ortuno, 2016	UK, Hospital	Cross-sectional	47 47% male	Mean (SD): 85.1 (5.8)	Single-item "Do you feel lonely" Yes/No	59.3%	Length of hospital stay (days)	Age SES[5] HC[7]	Length of hospital stay: β=0.38*	6

							Re-admission within 30 days of discharge		Re-admission: OR=0.61	
Lauder et al., 2004	Australia, Community	Cross-sectional	1241 50% male	Mean (SD): 45.1 (15.4)	11-item de Jong Gierveld Loneliness Scale	35.7%	GP visits	Not reported	RR=1.03, (95% CI: 0.98-1.07)	6
Lofvenmark et al., 2009	Sweden, CHF patients	Cross-sectional	149 52% male	Mean (SD): 76 (10.3)	Single-item "Does it happen that you experience loneliness?" Yes = always or often No = seldom or never	20.0%	Number of hospital re-admission Hospital stays within 1 year	Not reported	Hospital re-admission: lonely vs non-lonely individuals: mean (SD): 3.1(2.2) vs. 2.1 (1.6) * Hospital stays: lonely vs non-lonely individuals: mean (SD): 17(18.5) vs. 7.4(7.0)*	4
Molloy et al., 2010	Republic of Ireland and Northern Ireland, Community	Cross-sectional	2033 % male not reported	≥65	Single-item "How often in the last 12 months have you been bothered by loneliness?" Very often	11.0% "quite often" loneliness 4.0% "very	Emergency healthcare use during last 12 months Planned hospitalisation	Age Sex SES[6] HC[8] SF[2]	Emergency healthcare use: OR=1.29 (95% CI: 1.08-1.55) * Planned hospitalisation: OR=1.09	7

					Quite often Not very often Never	often" loneliness	during last 12 months		(95% CI: 0.92-1.28)	
Newall et al., 2015	Canada, Phase 3 of the Wellness Institute Services Evaluation Research study (WISER)	Longitudinal 2.5-year follow-up	954 46% male	Mean (SD): 63.5 (10.4) (range: 45-95) at baseline	Single-item "Participants were asked to categorize themselves as being not lonely, moderately lonely, severely lonely or extremely lonely" Grouped as not lonely or lonely for analysis	24.0%	Physician visits Hospitalisation Hospital re-admission Length of hospital stay	Age Sex SES[7] HC[9] SF[3]	Physician visits: RR=1.06 (95% CI: 0.95-1.18) Hospitalisation: OR=0.86 (95% CI: 0.61-1.21) Hospital re-admission for individuals who used to be hospitalized during follow-up: OR=1.74 (95% CI: 1.01-3.00) * Length of hospital stay: OR=1.09 (95% CI 0.64-1.87)	8
Russell et al., 1997	US, rural residents	Longitudinal four-year follow-up	3097 37% male	Mean: 74 (range 65-99)	4-item version of the revised UCLA	Mean (SD): 4.87 (1.39) (score	Nursing home admission	Age Sex SES[8] HC[10]	Loneliness score 5: OR=1.04,	9

					Loneliness Scale	range 4-12)		SF[4] PF[4]	score 6: OR=1.19, score 7: OR=1.34, score 8: OR=1.69, score (9-12): OR=3.25**	
Shaw et al., 2017	US, 2006, 2008 and 2010 waves of the University of Michigan Health and Retirement Study (HRS)	Longitudinal Median follow-up time: 4.5 years (range=1-7)	5270 43% male	≥65	3-items loneliness scale	55.3%	Monthly Medicare spending Monthly inpatient/ outpatient/skilled nursing facilities (SNF) spending	Age Sex SES[9] HC[11] PF[5]	Monthly Medicare spending: loneliness predicted a $63.70 reduction*** Inpatient care spending: loneliness predicted a $54.50 reduction: IRR =0.96* Outpatient care spending: loneliness predicted a $3.70	7

									reduction: IRR=0.96 SNF: loneliness predicted a $36.10 reduction: OR=1.2	
Taube et al., 2015	Sweden, Community	Cross-sectional	153 33% male	Mean (SD): 81.5 (6.4)	4-items Looking back over the last year, which response alternative corresponds best for you? On the whole, do you believe that you feel lonelier than others of your age? When you feel lonely, how strong is your feeling of loneliness?	60.0%	Inpatient care (i.e. acute and planned hospital admission, length of stay) Outpatient care (i.e. number of physician contacts, ED visits)	Not reported	Inpatient care: Values not given, but indicated that loneliness was not related to inpatient care service use Outpatient care: physician contacts: mean (SD): 23.2 (13.3)* ED visits: mean (SD): 1.3 (1.6)**	5

					Do you feel lonely nowadays?					

Note: # In Andren and Rosenqvist's articles (1985, 1987), although the methods of assessing loneliness were not described fully, loneliness was regarded as the primary risk factor. To provide the bigger picture related to loneliness, health and social care service utilisation, articles were included as long as they had loneliness as primary risk factor.

*: p<.05, **: p<.01, ***: p<.001, OR: odds ratio, RR: relative risk, IRR: incident risk ratio, CHF: coronary heart failure

SES: socio-economic factors apart from age, sex and race

(1): marital status, employment status and income, (2): marital status, income, education, dental insurance, (3) social class, housing tenure, residency, car access, living arrangement, feelings for partner status, (4) education, marital status, financial situation, health insurance, (5) living arrangement, (6) marital status, education, living arrangement, (7) education, living arrangement, (8) marital status, education, income, employment status, (9) marital status, education, household-level income, net worth, employment status, urban or rural status

HC: health conditions

(1): self-rated health, number of chronic diseases, weight, (2) ADL limitations, (3) disability, number of chronic diseases, somatization, (4) self-rated health in the past year, (5) self-rated health, number of chronic diseases, disability, (6) self-rated health, (7) dementia status, frailty, (8) depressive symptoms, chronic diseases, (9) self-rated health, number of chronic diseases, (10) prior nursing home admission, disability, self-rated health, number of chronic diseases, number of prescriptions, hospitalisation, number of doctor visits, (11) self-reported comorbidity, ADL limitations, substance use history, body mass index (BMI)

HB: health behaviour

(1,2): smoking status

PF: psychological factors

(1,3): depression, (2) stress, (4) cognitive impairment, morale, (5) depressive symptoms

SF: social factors

(1) social cohesion, social support, child proximity, (2) social participation, social support, (3) social participation, (4) social activity, social network, social support

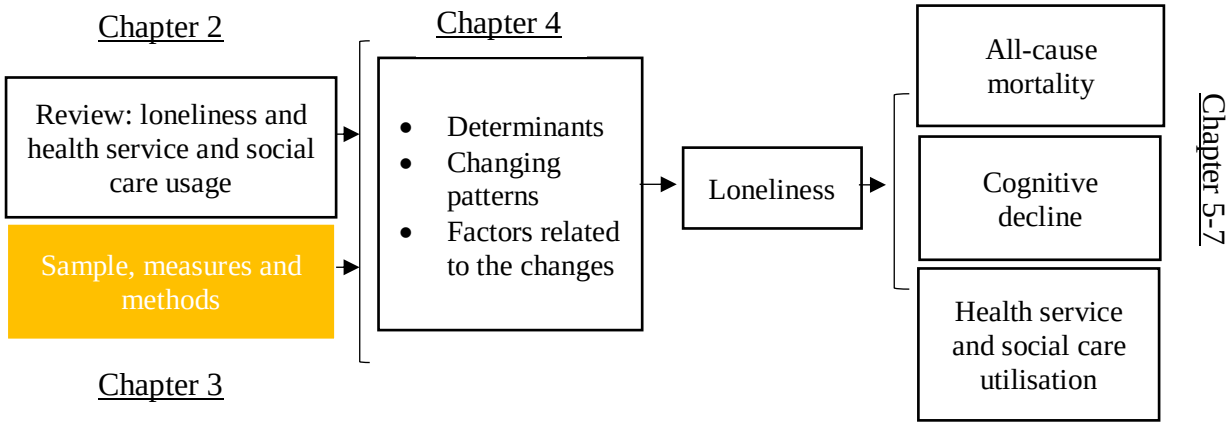
Chapter 3 Sample, Measures and Methods

3.1 Chapter Overview

The main research questions for this thesis were 'what factors are associated with loneliness in the oldest old' and 'how loneliness influences their health and healthcare service use'. Quantitative analyses of secondary data were appropriate methods to answer these questions.

On the other hand, as mentioned in Chapter 1, the conceptualisation of loneliness throughout this thesis was defined from researchers' perspective. To achieve a comprehensive view of loneliness, it is important to learn how laypeople articulate loneliness in their daily life. Because of the nature of qualitative research (e.g. it can contribute to epidemiological understanding by exploring conceptual and theoretical knowledge in depth), a qualitative study (i.e. an internet-based survey) was conducted to explore the cross-cultural perspectives of loneliness. However, as the main focus of this thesis is to fill research gaps with empirical evidence from quantitative data available, findings from the qualitative study are presented in Appendix. The CC75C study itself only introduced qualitative methods in the latter stages, focused on the experience of extreme age and proximity to death.

Overall, this chapter aims to introduce the cohort study used in this thesis, the Cambridge City over-75s Cohort (CC75C) study, to describe the main measures of variables and statistical methods used in subsequent analyses, and to explain reasons why specific statistical methods were used, as well as the reason to compute a cross-sectional weight for wave 3.


Chapter 2
Chapter 4
Review: loneliness and health service and social care usage
Sample, measures and methods
Chapter 3
Determinants
Changing patterns
Factors related to the changes
Loneliness
All-cause mortality
Cognitive decline
Health service and social care utilisation
Chapter 5-7

3.2 The Cambridge City over-75s Cohort (CC75C) study

The Cambridge City over-75s Cohort (CC75C) study is a population-based cohort study of the very old. The study began in 1985, and was designed to measure the prevalence, incidence and risk factors of cognitive decline and dementia (Fleming et al., 2007). The first wave included 2166 men and women aged 75 or older (2610 were initially targeted, 444 were further excluded due to different recruitments or participation in concurrent intervention studies) who were registered in the geographical area and socially representative of general practices in Cambridge; a 95% response rate was achieved from six of the seven practices. Follow-up interviews (hereafter refer to quantitative surveys where quantitative data were collected) were conducted with surviving participants every three or four years. For participants who were too frail, their proxy informants were interviewed in order to minimize dropping out rate and to keep the sample representative. In total, 10 waves' data have been collected (Figure 3.1).

Each follow-up survey included detailed cognitive function assessments, such as the Cambridge Cognitive Examination (CAMCOG) and the Mini-Mental State Examination (MMSE); participants towards cognitive decline have had additional psychiatric assessments using the Cambridge Diagnostic Examination for the Elderly (CAMDEX), neuropsychological assessment or other relevant tests. Apart from cognition assessments, data on socio-demographic factors (e.g. residency, household structure, marital status, social contact, social activities), activities of daily living, health conditions and use of medications, health and social service utilisation, self-rated health and subjective well-being were also collected at each wave.

Information on the vital status of each participant was obtained from the United Kingdom Office of National Statistics. Each phase of the CC75C study has been approved by the local Research Ethics Committee (i.e. the East of England-Cambridge Central Research Ethics Committee, a unique approval number was given for the whole study and for each study stage. For example, approval number for the whole study was 05Q0108/308; approval number for a descriptive study of functional ability, falls and fractures among the very olderly was LRE01/330, etc.). Participants were approached first by letter through their general practices at each study time. The

study's first six waves all pre-dated the Mental Capacity Act (MCA) after which the consent procedures were reviewed to ensure the whole process was in line with the latest legal requirement. The role of proxy informants, pre-2005 giving 'proxy consent', was in line with the MCA requirement for a 'consultee' to confirm, in instances when a participant with insufficient mental capacity to give fully informed written consent, that they are taking part in an interview willingly, understanding that any interview could be stopped if a participant appeared not to want to continue. Furthermore, participants' and proxy informants' consent was re-sought at each new wave and for the informant interviews after participants had died.

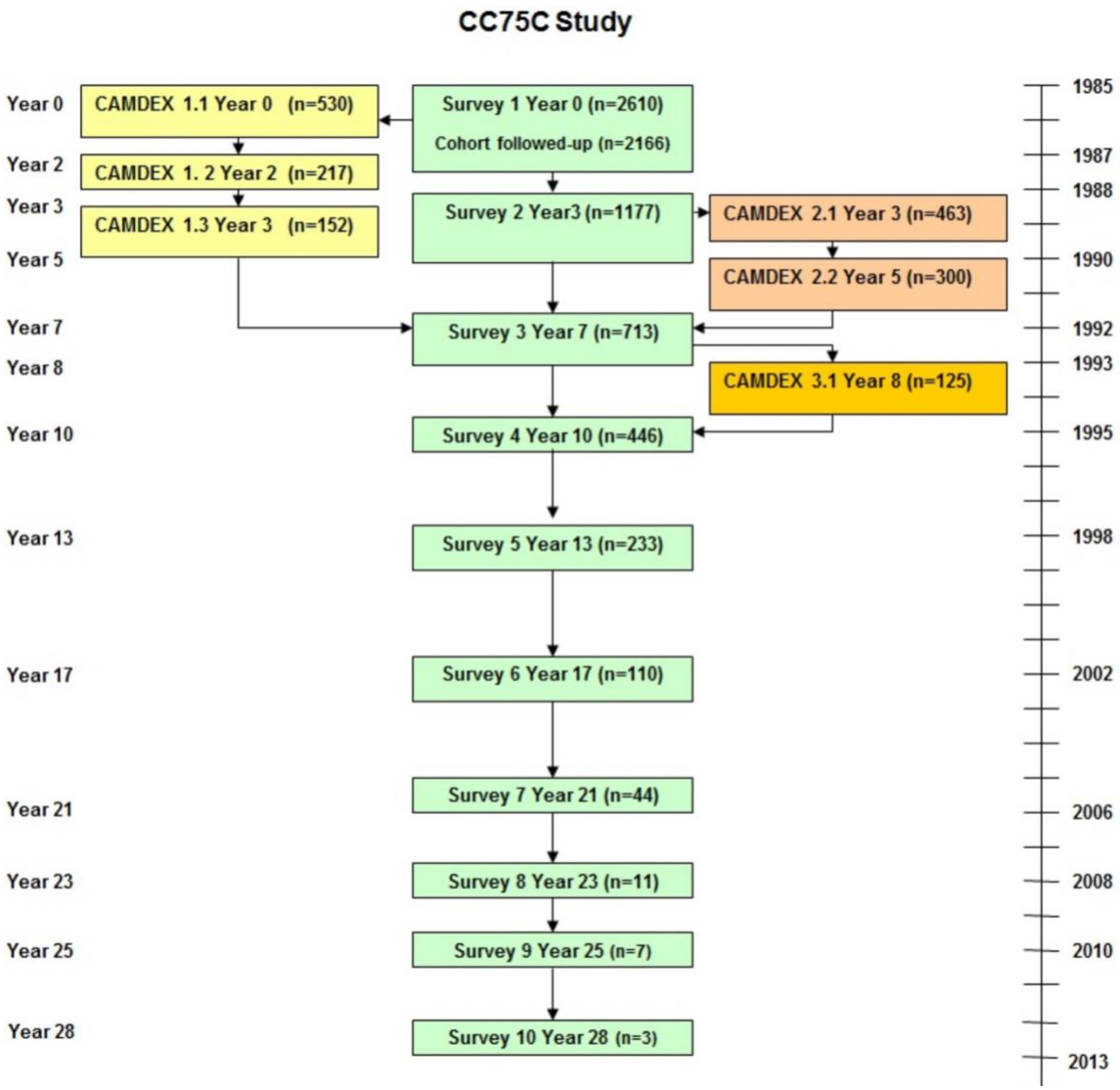


Figure 3. 1 Overview of the CC75C study

Data source: http://www.cc75c.group.cam.ac.uk/background/study-overview/

3.3 Main measures

The variables listed in this section are those used in all (or most) subsequent statistical analyses.

3.3.1 Loneliness

From wave 3 onwards, participants were asked "Do you feel lonely?" with possible answers: "very lonely", "lonely", "slightly lonely" and "not at all lonely". Due to the small frequency of the response option "very lonely" at each of these waves, the responses "very lonely" and "lonely" were combined as one category. Thus, loneliness was divided into three levels: "not lonely", "slightly lonely" and "lonely/very lonely", but for convenience the term "lonely" is used to refer to the combined "lonely/very lonely" category through this thesis. The single-item loneliness scale was widely used in European studies, and previous evidence has shown that the single-item measurement scale was well accepted by older people (Victor et al., 2005a).

3.3.2 Education

Education was measured at wave 1 by asking the question "How old were you when you left school?"; answers were recorded in years. It was further dichotomized into two levels: *0=left school before age 15, 1=left school at 15 or after* by survey investigators. Only the categorical format of 'education' was given when accessing to the dataset.

3.3.3 Social class

Social class was assessed at wave 1 by asking participants' (for women, their husband's) occupation; answers were coded into social class classifications following the Registrar General's Scale of Social Class and Socio-economic Groups. A total of 6 major classes were identified ranging from "Professional" in class one to "Unskilled" and "Other" in class 5 and 6. Class 3 was sub-divided into manual and non-manual skills. For the ease of analysis, social class was further dichotomized into *0=manual social class and 1=non-manual social class*, with *manual social class*

consisting of skilled (manual), partly skilled and unskilled social classes and *non-manual social class* including professional, managerial/technical and skilled social classes.

3.3.4 Health conditions (number of self-reported doctor-diagnosed diseases)

Health conditions were measured at each wave through a series of self-reported doctor-diagnosed chronic diseases including angina, heart attack, problems with circulation in legs, high blood pressure, chronic bronchitis, stroke, sudden weakness or difficulty with speech, memory or vision, diabetes, thyroid problems, severe headaches or migraine and others; answers were categorised into 0-2 or ≥3 conditions based on median.

3.3.5 Depression

Depression was assessed at each wave by a series of questions (10 questions) derived from the Cambridge Examination for Mental Disorders in the Elderly (CAMDEX) (Roth et al., 1986) whose diagnostic criteria for depression is reported to be virtually identical to DSM-III criteria for major depressive disorder (American Psychiatric Association, 1980). The total score for depression was the sum of the score of each question, which ranged from 0-10. Depression was defined if score ≥6. The validity and reliability of defining depression was tested within the CC75C population (Girling et al., 1995).

3.3.6 Physical functioning

Physical functioning categorised participants by their responses to questions on activities of daily living (Lawton and Brody, 1969) as *no disability*, *Instrumental ADL disability only (IADL disability)* or *disability in both basic ADLs and IADLs (ADL and IADL disability)*. The score was derived from responses to four basic ADL measures (bathing, dressing, getting to the toilet on time and grooming), and two IADL measures (cooking and housework). If study participants did not need help in any of these six activities, then they were assigned to no disability group; if study participants needed help with either cooking or housework or both, then they were

rated IADL disability; if study participants needed help with any of the four basic ADL activities, then they were rated ADL and IADL disability. The reason of selecting cooking and housework as the measure of IADLs was that there two items were measured consistently across surveys of the CC75C study with the least missing data.

3.3.7 Cognition

The assessment of cognition was based on the Mini-Mental State Examination (MMSE) (Folstein et al., 1975). The MMSE examines cognition from four domains including orientation, immediate and short-term memory, attention and calculation, language and praxis. The total score of MMSE is 30 with higher score reflecting better cognition; a score of 23 or less is generally accepted as indicating cognitive impairment. The construct validity of MMSE has been tested in previous studies and found to be adequate (Lancu and Olmer, 2006).

In CC75C, when scoring MMSE test at each wave, the refused or missed items that were due to participants' sensory or physical difficulties were coded to 0, as were the items that were due to "Not asked", "Do not know" or "Refusal". Since there were no assumptions made about those items, MMSE score may underestimate the true cognitive function. However, the total number of MMSE item missingness within this regard was very small, and could not impact the overall estimations of cognitive function. The MMSE score was categorized into four levels: normal cognition (score 26-30), mild cognitive impairment (score 22-25), moderate cognitive impairment (score 18-21) and severe cognitive impairment (score 0-17). The reliability and validity of this coding on MMSE was tested in CC75C study (O'Connor et al., 1989). In analysis, due to the small frequency of participants who had moderate and severe cognitive impairments, these two categories were further combined as one category: moderate-severe cognitive impairments. Depending on research questions and statistical models, the MMSE score was used either as a continuous variable (score 0-30) or a categorical variable in analyses.

3.4 Statistical analyses

The aim of this section is to introduce methods that are used in statistical analysis in the thesis, reasons why choosing them and some of the issues related to these methods. Detailed descriptions are provided within corresponding chapters.

3.4.1 Cross-sectional modelling

Briefly, cross-sectional designs are commonly used to measure the prevalence of health outcomes or the associations between risk factors and health in a population at one point in time or over a very short period. It is like a "snapshot" of population being studied at a given point in time.

3.4.1.1 Proportional odds model

Proportional odds model is a commonly-used method for analysing data with categorical ordinal outcomes. Loneliness is an ordinal outcome, it is therefore appropriate to consider proportional odds model to explore risk factors of loneliness. However, prior to using this model, the assumption of proportional odds (also called parallel lines assumption) has to be satisfied. The proportional odds assumption can be explained as the effect of an independent variable (IV) being identical over all of the levels of the dependent variable (DV). In other words, a one-unit increase in an IV has the same effect on the probability of a response being in a higher category regardless of category.

The assumption can be tested by a series of logistic regression analyses on binary versions of the ordinal DV (O'Connell et al., 2006). For example, if the DV measures the opinion of whether working women should spend at least 2 hours at home per day to take care of housework and has five levels: 1=strongly disagree, 2=disagree, 3=neutral, 4=agree and 5=strongly agree; the IV is gender measurement and categorized into: 0=female and 1=male, then odds ratios (OR) that examine the association between gender and opinion can be calculated by:

The first (OR) is based on a comparison of category 1 with categories 2, 3, 4 and 5.

$$OR = \frac{\left[\frac{P(Y > 1|x_1)}{1 - P(Y > 1|x_1)}\right]}{\left[\frac{P(Y > 1|x_0)}{1 - P(Y > 1|x_0)}\right]} \quad (3.1)$$

The second OR is based on a comparison of categories 1 and 2 versus categories 3, 4 and 5.

$$OR = \frac{\left[\frac{P(Y > 2|x_1)}{1 - P(Y > 2|x_1)}\right]}{\left[\frac{P(Y > 2|x_0)}{1 - P(Y > 2|x_0)}\right]} \quad (3.2)$$

The third OR is based on a comparison of categories 1, 2 and 3 versus categories 4 and 5.

$$OR = \frac{\left[\frac{P(Y > 3|x_1)}{1 - P(Y > 3|x_1)}\right]}{\left[\frac{P(Y > 3|x_0)}{1 - P(Y > 3|x_0)}\right]} \quad (3.3)$$

The fourth OR is based on a comparison of categories 1, 2, 3 and 4 versus category 5.

$$OR = \frac{\left[\frac{P(Y > 4|x_1)}{1 - P(Y > 4|x_1)}\right]}{\left[\frac{P(Y > 4|x_0)}{1 - P(Y > 4|x_0)}\right]} \quad (3.4)$$

where $P(Y > j|x_i) = P_{ij} = \frac{e^{(\alpha_j + x_i\beta)}}{1+e^{(\alpha_j + x_i\beta)}}$ is the probability of DV level (j) for a given independent variable (X_i); j indicates the level of DV, J = the number of DV levels -1; X_i indicates the independent variable.

In this example, the assumption of proportional odds will be satisfied if ORs from the above equations are identical.

3.4.1.2 Partial proportional odds model

However, not all cases can meet the proportional odds assumption. When the assumption is violated, the partial proportional odds model can be considered. The partial proportional odds model (PPO) has been regarded as an intermediate method bridging the gap between proportional odds model and multinomial models (these completely ignore the sequential order of the dependent variable) (Sasidharan and Menendez, 2014). The proportional odds assumption is relaxed in the PPO model as PPO allows a combination of the proportional and multinomial modelling frameworks. Two subsets of independent variables are identified in PPO; one subset includes independent variable(s) that can satisfy the proportional odds assumption, and the other includes independent variable(s) that will reject the assumption (Peterson and Harrell, 1990).

3.4.2 Longitudinal modelling

Longitudinal studies repeat measurements of the same thing in participants over time. Therefore, it has the ability to estimate changes in health-related variables, and these assessments of change within a cohort can provide valuable information for medical researchers, clinicians, and even policy makers. Statistical methods used to model these associations are called longitudinal methods.

3.4.2.1 Multi-state model

A multi-state model illustrates how an individual moves between a series of different states in continuous time. Figure 3.2 shows a three-states multi-state model. The transitions between discrete state (e.g. 1,…,N) is guided by transition intensities q_{rs}(t, z(t)) (detailed information about transition intensity is in section 3.4.2.1.3): r, s=1,…N. The intensity is the instantaneous risk of transferring from state r to state s in which r≠s. It can be influenced by time or a set of explanatory variables z(t) (Equation 3.5).

$$q_{rs}\big(t, z(t)\big) = \lim_{\partial_{t\to 0}} P(S(t+\partial_t) = s | S(t) = r))/\partial_t \quad (3.5)$$

Generally, multi-state models can be divided into three sub-models according to the dependence of the transition rates on time, which include (1) time homogeneous model: the intensities are independent of time, (2) Markov model: the future evolution only dependent on the current state, and (3) Semi-Markov model: future evolution not only dependent on the current state s, but also on the entry time t_s into state s (Meira-Machado et al., 2009). Because of the simplicity, the Markov multi-state model has been used frequently in epidemiology and medical research to model the course of diseases and was used here.

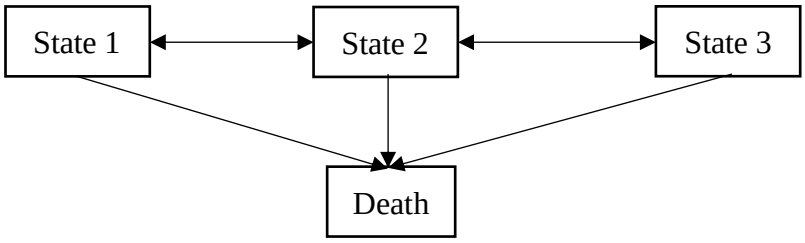


Figure 3. 2 A description of three-states multi-state model

Note: death is an absorbing state. In Markov Chain modelling, an absorbing state is a state that individuals can enter but cannot leave.

3.4.2.1.1 Markov multi-state model for longitudinal data

In longitudinal studies, participants are usually interviewed at scheduled follow-up times (arbitrary observation times) during which data are collected, and contemporary information from the time periods between visits is not available. Therefore, the exact time of disease onset is unknown and the changes of state in a multi-state model usually occur at unknown times. Additionally, drop out can occur at any stage in the study and if it occurs early in the study only a short period of disease development process can be captured. Figure 3.3 shows a typical longitudinal sampling framework. In this example, a participant is observed at five visits through 12 months. The final record is the death date. The available information is the occupation of states 2, 2, 1, and 3 at time 2, 4, 6, 8 months, respectively. The times of transitions between states and the exact length of state occupancy in between the observation times are unknown.

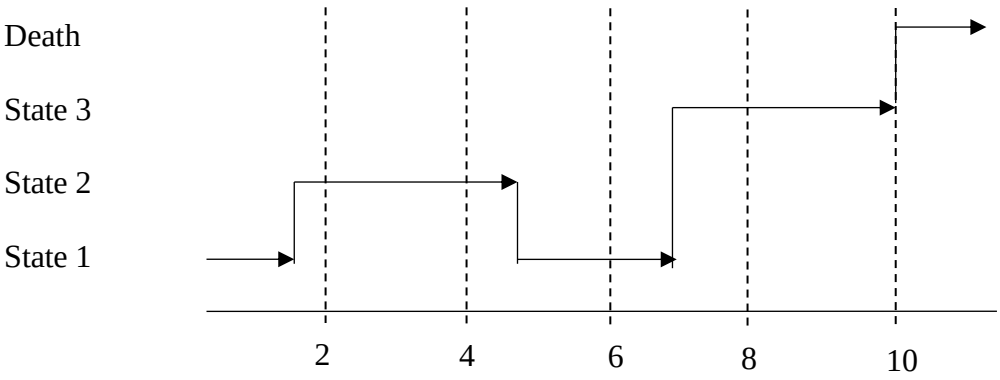


Figure 3. 3 A process illustrating a participant is observed at five visits

3.4.2.1.2 Probability transition matrix

The transition probability matrix is the N*N matrix with P(t) denoted as the probability of entering in row i and column j ($n \geq i, j \geq 1$) (Equation 3.6).

$$P(t) = \begin{pmatrix} P_{11}(t) & \cdots & P_{1n}(t) \\ \vdots & \ddots & \vdots \\ P_{n1}(t) & \cdots & P_{nn}(t) \end{pmatrix} \quad (3.6)$$

Each element (i.e. $P_{ij}(t)$) in the transition probability matrix indicates the probability of being in state s at time $t+t_0$, conditional on being in state r at time t_0 (Markov assumption). This matrix does not reflect whether the process has entered into other states between time t_0 and $t+t_0$ or not. It should be noted that for each transition probability, the value should be equal to or greater than zero, and the sum of the probabilities in each row is equal to 1 (Jackson, 2011).

3.4.2.1.3 Transition intensity matrix

As noted in section 3.4.2.1, the transition intensity $q_{ij}(t, z(t))$ is the guidance for the movement between discrete states. It is the change rate of the probability P_{rs} in a very short time interval. The matrix is donated as Q with a dimension of N*N ($n \geq i, j \geq 1$) (Equation 3.7).

$$Q = \begin{pmatrix} q_{11} & \cdots & q_{1n} \\ \vdots & \ddots & \vdots \\ q_{n1} & \cdots & q_{nn} \end{pmatrix} \quad (3.7)$$

The parameter q_{ij} represents the intensity of the process entering row i and column j. The sum of each parameter in each row equals zero, and the parameters in the diagonal need to be equal to the negative sum of the parameters in that specific row. An example is shown in Equation 3.8.

$$Q = \begin{pmatrix} -(q_{12} + q_{13}) & q_{12} & q_{13} \\ q_{21} & -(q_{21} + q_{23}) & q_{23} \\ q_{31} & q_{32} & -(q_{31} + q_{32}) \end{pmatrix} \quad (3.8)$$

The above matrix is a 3*3 matrix. The off-diagonal parameters represent the rates at which the process is moving into other states, while the diagonal parameters represent the rates at which the process remains in that specific state (Jackson, 2011).

3.4.2.1.4 Maximum likelihood estimation

The parameters of the Markov multi-state model are estimated by using maximum likelihood estimation. Given the observations, the maximum likelihood estimation is equal to the number of transitions from state r to state s divided by the number of overall transitions from state r to other states. In multi-state model, this can be calculated from the transition probability matrix P(t) (Jackson, 2011).

3.4.2.1.5 Censor state

In survival studies, the most common censor state is right censoring, which means that individuals are alive at the time the study ended. In other words, the time of death is greater than the end time of the study. In multi-state model, the censor state means the times of changes of states are unknown, but known to be within intervals. For instance, in a study of back pain, let 0=no pain, 1=slightly painful, 2=painful and 3=extremely painful; transitions between different levels of back pain are allowed. If, when modelling the transitions, the exact level of back pain for a participant is unknown, but known to be within stage 2 and stage 3, then the likelihood for this individual is a sum of the likelihoods of paths through all unobserved states (e.g. from stage 1 to stage 2 and from stage 1 (to stage 2) to stage 3; although transition from

state 1 to state 3 is observed, in multi-state model, it specifies that transition from state 1 to state 3 must have passed through state 2) (Jackson, 2011).

3.4.2.1.6 Covariates

As noted in section 3.4.2.1, the transition intensity can be influenced by covariates. Sometimes, covariates are time-varying (time-dependent) variables. In this situation, time-varying covariates are assumed to be piecewise-constant (Jackson, 2011). Models with transition intensities which are piecewise-constant in time are called time-inhomogeneous. For a time-inhomogeneous model, the transition probability varies with time-varying covariates, and can be approximated as piecewise-constant.

3.4.2.1.7 Misclassification

Misclassification can occur in Markov disease progression models (Jackson, 2011). For example, when screening for the presence of a disease, the screening results may not always reflect the true prevalence of the disease as the screening process can be subject to errors. In other words, the observed state for participant i at time (t) does not equal to the true state for this participant at time (t). The probability of misclassification can be calculated by:

$$P\left(Q\left(t_{ij}\right)\right) = s/S\left(t_{ij}\right) = r \quad (3.9)$$

where $Q(t_{ij})$ is the observed states for participant i at time t_j, whereas $S(t_{ij})$ is the true states for individual i at time t_j.

3.4.2.1.8 Model assessment

Assessing the suitability of a model is very important; for example, the test of validation of a model assumption before conducting statistical analyses is essential to avoid misleading inference and conclusions. The following sub-sections describe two general measures of goodness-of-fit for a multi-state model: informal and formal. The detailed information about these assessment tools can be found in the work by

Gentleman et al. (1994), Aguirre-Hernandez and Farewell (2002) and Titman and Sharples (2008).

3.4.2.1.8.1 Informal goodness-of-fit assessment

An informal goodness-of-fit can be conducted by comparing the fitted data with observed data. In an ideal model, the fitted data (i.e. the numbers or frequencies in each state) can be assessed directly at times at which all participants are observed. However, in practice that is not the case. If data from all participants cannot be observed, then approximations need to be made (Jackson, 2011). For example, if a participant's state at an arbitrary time t is unknown, then the state at time t can be assumed to be the same as the state at the previous observation time. The problem with this assumption is that if the time intervals between observations are too large, then the assumption will be less likely to reflect the true transition, leading to less accurate results.

3.4.2.1.8.2 Formal goodness-of-fit assessment

Similar to the classical Pearson's chi-square test for contingency tables, the formal goodness-of-fit assessment for the multi-state model, Pearson-type goodness-of-fit test, needs to construct tables of observed and fitted number of transitions (Jackson, 2011). The observed and fitted transitions are defined by:

$$O_{thrscg} = \sum E(S(t_{i,j+1}) = s, S(t_{ij}) = r) \quad (3.10)$$

$$F_{thrscg} = \sum P(S(t_{i,j+1}) = s, S(t_{ij}) = r) \quad (3.11)$$

where E() is the indicator function for an event, it is the summary of transitions defined by t, h, r, s, c, and g; t indicates the time between the start of the process and the first of the pair of observations (transition), h is the time interval between the observations, r and s indicate the starting state and finishing state, c indicates the effects of covariates and g indicates any other factors of interest for diagnosing lack of fit. The Pearson-type test is then given by:

$$D = \sum_{thrscg} \frac{(O_{thrscg} - F_{thrscg})^2}{F_{thrscg}} \quad (3.12)$$

The Pearson-type test has a distribution of x^2_{n-p}, where n indicates the total number of independent cells in the table and p is the number of estimated parameters. Because the time intervals between transitions are not always identical, the distribution of the statistic does not exactly follow the distribution of x^2_{n-p}. In fact, it is reported that the distribution lies between x^2_n and x^2_{n-p}; consequently, the p-value of the statistic can be calculated from the distribution of x^2_n and x^2_{n-p} (Aguirre-Hernandez and Farewell, 2002; Titman, 2009).

In the current study, loneliness (and cognition) contains different levels, transitions between different levels are allowed and assumed to be affected by risk factors; therefore, multi-state model is considered to be a proper analytic technique to investigate the predictors of loneliness (and cognitive) transitions.

3.4.2.2 Cox regression model

The Cox regression model (also named Cox proportional hazards model) is the most commonly used statistical approach for analysing survival data in medical research. It describes the relationship between the event incidence and a set of covariates. In the Cox regression model, the event incidence is represented by the hazard function, where the hazard is the probability that an individual under observation develops the event at a given time (Cox, 1972). The Cox regression model can be defined by:

$$h(t) = h_0(t) \times \exp(b_1 x_1 + b_2 x_2 + \cdots + b_n x_n) \quad (3.13)$$

where h(t) is the hazard function and dependent on a set of covariates $(x_1, x_2, \dots, x_n)$; t means that the hazard function varies over time; $b_1, b_2, \dots\ b_n$ is the coefficient and represents the size of the impact of covariates on hazard function; $h_0(t)$ is the baseline hazard, the hazard will be equal to the baseline hazard when all covariates equal to 0 ($e^0 = 1$).

3.4.2.2.1 Cox regression model with time-varying (time-dependent) covariates

One of the strengths of the Cox regression model is its ability to model time-varying covariates. It is because the Cox regression model compares the current covariate values of the individual who experienced the event to the current values of all others who were at risk at the event time. The key assumption for the Cox regression model with time-varying covariates is that the current hazard depends only on the past, it cannot reach forward in time as described below.

The typical way to construct time-varying covariates in the Cox regression model is to split data into equal time (or based on data collection framework) intervals with one row of data for each interval (Therneau et al., 2013). Here is an example of testing the impact of drug A (ug/dl) on development of cardiovascular disease (CVD) over 90 days:

$Visit$	$Subject$	$time1$	$time2$	CVD	$drug\ A$
1	1	0	30	0	1.2
2	1	30	60	0	1.5
3	1	60	90	1	1.8

As can be seen, the amount of drug A consumption is measured at day 30, 60 and 90, which takes values of 1.2, 1.5 and 1.8, respectively. For subject 1, the amount of drug A consumption was 1.2 at day 30, and there was no sign of developing CVD; the amount of drug A consumption was 1.5 and the subject remained CVD-free at day 60. At day 90, the subject was found to have developed CVD, and the consumption of drug A was 1.8. Since the model cannot look into future evolution, the model cannot predict a value of drug A consumption on day 55, because on day 55 the drug A value of 1.5 has not yet been obtained.

3.4.2.3 The generalized estimating equations (GEE) model

GEE is a marginal approach (i.e. population-averaged model) to examine the relationships between the variables of the model at different time points by using all available longitudinal data. The outcome variable can take forms of continuous, category or count. Detailed information about GEE can be found in the work by Liang

and Zeger (1986). The following equation describes the general form of GEE (Equation 3.14). In this equation, β_{ij} represents the longitudinal relationship between the outcome variable Y and the corresponding covariate X for individual i at jth visit, t indicates time, ε_{it} is an error term and the $corr_{it}$ reflects the correlation between observations.

$$Y_{it} = \beta_0 + \sum_{j=1}^{J} \beta_{ij} x_{ijt} + \epsilon_{it} + corr_{it} \quad (3.14)$$

In longitudinal studies, because the collected data have temporal ordering and dependence between consecutive measures, an adjustment for these is required (Diggle et al., 2002). In GEE, the adjustment is conducted by assuming a prior "working" correlation structure for the repeated measures of outcome variable, which includes independence, exchangeable, autoregressive and unstructured (Table 3.1).

Table 3. 1 Summary of different "working" correlation structures in GEE model

GEE Model			
Independence	**Exchangeable**	**Autoregressive**	**Unstructured**
The correlations between measurements are assumed to be zero.	The correlations between measurements are assumed to be equal.	The correlations one measurement apart are assumed to be ρ; the correlations two measurements apart are assumed to be ρ^2; the correlations m measurements apart are assumed to be ρ^m.	The correlations between measurements are assumed to be different.
$\boldsymbol{C} = \begin{bmatrix} - & \mathbf{0} & \mathbf{0} \\ \mathbf{0} & - & \mathbf{0} \\ \mathbf{0} & \mathbf{0} & - \end{bmatrix}$	$C = \begin{bmatrix} - & \alpha & \alpha \\ \alpha & - & \alpha \\ \alpha & \alpha & - \end{bmatrix}$	$C = \begin{bmatrix} - & \alpha^1 & \alpha^2 \\ \alpha^1 & - & \alpha^1 \\ \alpha^2 & \alpha^1 & - \end{bmatrix}$	$C = \begin{bmatrix} - & \alpha_1 & \alpha_2 \\ \alpha_1 & - & \alpha_3 \\ \alpha_2 & \alpha_3 & - \end{bmatrix}$

Although it has been reported that the results from GEE with a wrong choice of the correlation structure are robust, it is only in the case where there are no missing data in the model. Unfortunately, there is no straightforward way to determine which correlation structure should be used. One possible way to estimate the correlation structure is to analyse the within-subject correlation structure of the observed data. In practice, the simplest correlation structure is used first (i.e. independence structure),

and based on the residuals of this analysis, the parameters of the working correlation structure can be calculated.

3.4.2.3.1 Model selection

The GEE model uses the quasi-likelihood estimations. The model comparison is therefore based on the criteria of quasi-likelihood under the model with independence "working" correlation structure (QIC). In other words, QIC compares models with different correlation structures; the smaller the QIC, the better the model.

3.4.2.3.2 GEE model modelling count dependent variable

The count variable is a special type of categorical variable; it takes discrete and non-negative values, such as 0, 1, 2, … n. Because of this nature, it is assumed to follow a Poisson distribution.

3.4.2.3.2.1 GEE with Poisson family (Poisson model)

The Poisson model was developed to model the discrete count data. To implement this model, data have to meet two assumptions: (1) the mean and variance of the count data have to be equal and (2) the occurrences of specific events are assumed to be independent of each other.

3.4.2.3.2.2 GEE with negative binomial family (negative binomial model)

In practice, the variance of data is not always equal to (usually greater than) the mean (i.e. overdispersion). In addition, the second assumption is much often violated. For example, the occurrence of current suicidal attempts is more likely to be related to past suicidal attempts. The distribution of the negative binomial model is similar to that of the Poisson model, but it relaxes the assumptions in the Poisson model; it can model overdispersion well, and does not need the independence of observations.

3.4.2.4 Attrition in longitudinal study

Attrition is unavoidable in longitudinal studies; it can be defined as the loss of study participants after the original study population has been defined. Generally, there are three types of attrition: death, contact failure and non-response including inability to continue to respond or refusal to respond. In this thesis, the dropout indicates the loss of follow-up that is not due to death.

Two dropout patterns have been proposed: (1) a subject can drop from one wave and return to the study later and (2) a subject drops from one wave and never returns to the study. The second pattern is commonly encountered in longitudinal studies, and named "monotone" dropout. Subsequent analyses will focus on "monotone" dropout. Either death or dropout can lead to missing data problems; analyses with incomplete data are likely to produce biased results. The next section will discuss the mechanisms of missing data and the potential statistical approaches to dealing with missing data.

3.4.2.5 Missing data

Three types of missing data have been proposed: missing completely at random (MCAR), missing at random (MAR) and missing not at random (MNAR) (See Table 3.2) (Little and Rubin, 2002).

Table 3. 2 Summary of missing data types

Missing data		
Types	**Definition**	**Example**
MCAR	No systematic differences between missing data and observed data.	Sleep quality measurement is missing because the device that is assessing the quality of sleep is broken.
MAR	Differences between missing data and observed data can be explained by differences in observed data.	Missing data on sleep quality is worse than measured data only because older people may be more likely to have their sleep quality measured.
MNAR	Differences between missing data and observed data remain even after taking into account the differences in observed data.	Subjects with bad sleep quality are more likely to have missing data on sleep because they have impaired memory functions.

A variety of approaches have been developed to deal with missing data. These approaches are generally categorised into: complete case analysis, single imputation methods (e.g. last values carried forward, mean substitution), multiple imputation, inverse probability weighting, etc., of which multiple imputation and inverse probability weighting are the mostly widely used approaches and are suitable under MAR. For data that is MNAR, sensitivity analysis is recommended to ensure the validity of results. In practice, there is no valid way to test the missing mechanisms, and the assumption of MCAR, MAR or MNAR is based on the observed data.

3.4.2.5.1 Multiple imputation

Multiple imputation creates multiple datasets that reflect the original complete data. The imputation process is based on observed values. If M complete data sets are created, then statistical analysis can be conducted with each of the M data sets. Results from M analyses will be integrated, a pooled result will be given (Figure 3.4). It has been suggested that five imputed data sets are adequate (Schafer, 1999), however, recently this has been questioned by other researchers (Graham et al., 2007). Multiple imputation works well if auxiliary variables (i.e. variables that are not used in statistical analysis, but are correlated to the outcome variable or related to missingness) are included in the imputation process (Hardt et al., 2012). The detailed information about multiple imputation and relevant issues can be found in a recent review (Sterne et al., 2009).

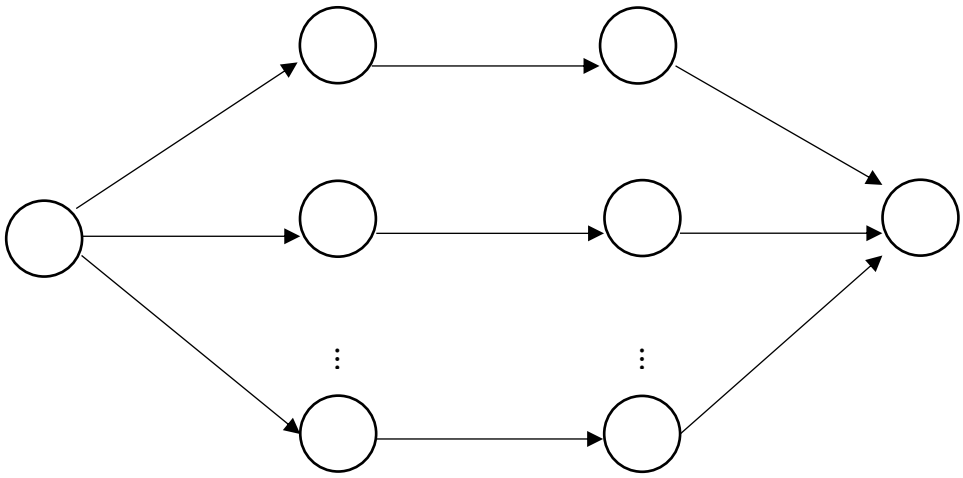


Figure 3. 4 The illustration of multiple imputation process

3.4.2.5.2 Inverse probability weighting

Within the inverse probability weighting approach, if an observation has a probability ρ of being observed, then this observation should be given a weight $1/\rho$ in the analysis (Mansournia and Altman, 2016). In longitudinal data with monotone dropout, if the probability of dropping out from wave t for subject i is d_{it} then the probability of remaining ρ_{it} in this study at wave t=1,2,…T can be expressed by:

$$\begin{aligned} \rho_{i1} &= 1 - d_{i1}; \\ \rho_{i2} &= (1 - d_{i1}) * (1 - d_{i2}); \\ \rho_{it} &= (1 - d_{i1}) * (1 - d_{i2}) \cdots (1 - d_{it}) \end{aligned} \tag{3.15}$$

Apart from dealing with missing data, inverse probability weighting can also be used to correct for unequal sampling probabilities. For example, in a national survey exploring the prevalence of cardiovascular disease (CVD), individuals with rare characteristics (e.g. people aged ≥60 years) are usually oversampled to improve the precision of estimations for that group.

3.4.2.6 Target of inference

One philosophical question arises in longitudinal studies, that is, should deaths be taken into account when estimating mean levels of health-related variables over time? The answer is dependent on the study aims (Kurland et al., 2009). For example, if the study aims to describe a population as it was defined at the initiation of the study, then this implies an immortal cohort and subjects who die during follow-up will continue to be implicitly included; on the contrary, if the study aims to describe a population as it existed at each stage of the study, then it suggests a mortal cohort where deceased subjects are excluded after death. Based on study aims and research questions mentioned in Chapter 1 (section 1.5), this thesis will focus on mortal cohort only. Consequently, statistical methods that are suitable for modelling mortal cohort will be considered. The following table lists several statistical methods that are commonly used in longitudinal studies based on assumed attrition and missing data mechanisms.

Table 3. 3 Description of commonly used methods in immortal and mortal cohorts

Immortal Cohort	Explanation
Linear mixed model	Participants are implicitly included after death. Appropriate under MCAR or MAR.
Linear increment model	Assume that responses from participants would have been observed if they had continued in the study.
Joint model for longitudinal outcome and time-to-event (e.g. death)	It consists of two sub-models: a longitudinal sub-model (e.g. linear mixed model) and a time-to-event sub-model (e.g. Cox regression model). Appropriate under MNAR.
Mortal Cohort	**Explanation**
GEE with an independent working correlation structure	Inverse probability weighting needs to be conditional on responding to the previous wave and surviving to the current wave. The target population is individuals who are alive at each wave.
Multiple imputation	Valid for mortal cohort if re-set all the imputed values to missing for participants after death. Appropriate under MAR or MNAR.

Note: Information in above table was extracted from *"Analytical results in longitudinal studies depended on target of inference and assumed mechanisms of attrition"* by Jones et al., 2015.

3.5 Computing cross-sectional weight

Because loneliness is measured from wave 3 and onwards, wave 3 is regarded as the baseline data for empirical analyses. However, as wave 3 was conducted about 7 years after wave 1, participants who tended towards health decline were more likely to die or dropout. In addition, a few participants towards cognitive impairments went through detailed cognitive assessments and did not participate in wave 2, but some of them returned for wave 3. To account for complex participation, a cross-sectional weight was calculated. The weight will be used in subsequent analyses where necessary. The detailed calculating procedure can be found in Appendix 3.1.

3.6 Conclusion

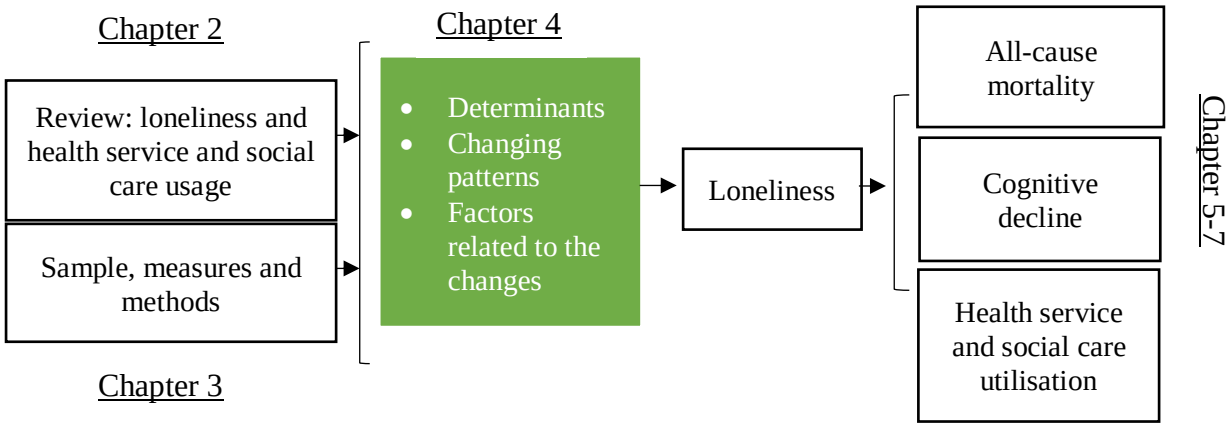
This chapter describes the study sample, introduces the main variables and provides the major statistical methods used in Chapters 4-7. The CC75C is a population-based cohort study including participants aged 75 or older. The data collected in CC75C cover a wide range of individual-level factors, including objective measures of socio-demographic characteristics, social contacts, cognition evaluations, and subjective measures of personal attitudes about social relationships, physical health, ageing process. These data provide a unique opportunity to explore loneliness in a representative population of the oldest old.

This chapter also describes the common issues related to longitudinal modelling, such as loss-of-follow-up and missing data, and provides possible solutions to deal with these issues. Based on this chapter, the next chapter will explore the determinants of loneliness in the oldest old, investigate the changing patterns of loneliness over time, and examine what individual-level factors predict changes.

Chapter 4 Loneliness, its risk factors, change with ageing and factors related to loneliness transitions in the oldest old

4.1 Chapter Overview

This chapter examines loneliness itself within the cohort including the investigation of associated risk factors, changes in loneliness over a 7-year follow-up, and factors related to loneliness changes over time. The examination of the potential risk factors of loneliness draws on data from wave 3; the investigation of changing loneliness and exploration of factors related to any changes observed draws on data from wave 3 to wave 5.



4.2 Introduction

Many conceptual frameworks have been developed to explore the associations between individual level factors and loneliness. Fees and colleagues hypothesized that mental health problems (i.e. cognition), personality (conceptualised as anxiety) and number of social contacts predicted loneliness, and physical well-being served as a mediator because decline in physical health was a dominant issue in older people (Figure 4.1) (Fees et al., 1999). Cohen-Mansfield and Parpura-Gill developed a model of depression and loneliness (MODEL) which was rooted in a cognitive-behavioural theory in which the feeling of loneliness may result from an interaction of cognitive processes and environmental factors (Figure 4.2) (Cohen-Mansfield and Parpura-Gill, 2007). Hawkely and colleagues proposed a filtration model in which distal factors (e.g. demographic characteristics) operate through proximal factors (e.g. income, education, health, social network size, quality of social relationships) to influence loneliness (Figure 4.3) (Hawkley et al., 2008). Heylen proposed a social relationship framework to explore the underlying mechanisms of quantitative and qualitative social relationships on loneliness (Figure 4.4) (Heylen, 2010). The model proposed in this chapter shares risk factors with each of above models; however, the current model was based on a larger conceptual framework that contains a more diverse range of risk factors and assesses the direct impact of risk factors on loneliness (Figure 4.5).

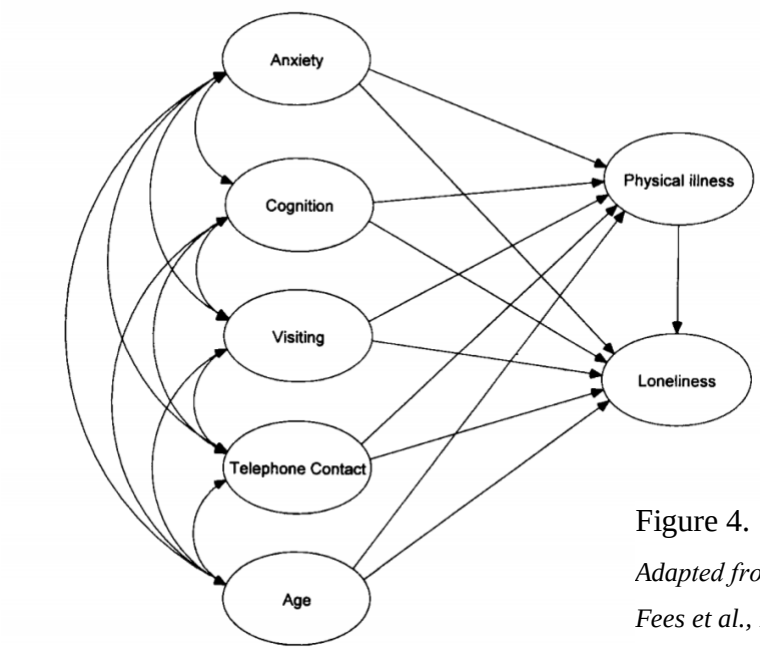


Figure 4. 1 Physical health mediated model

Adapted from "A model of loneliness in older adults" Fees et al., 1999.

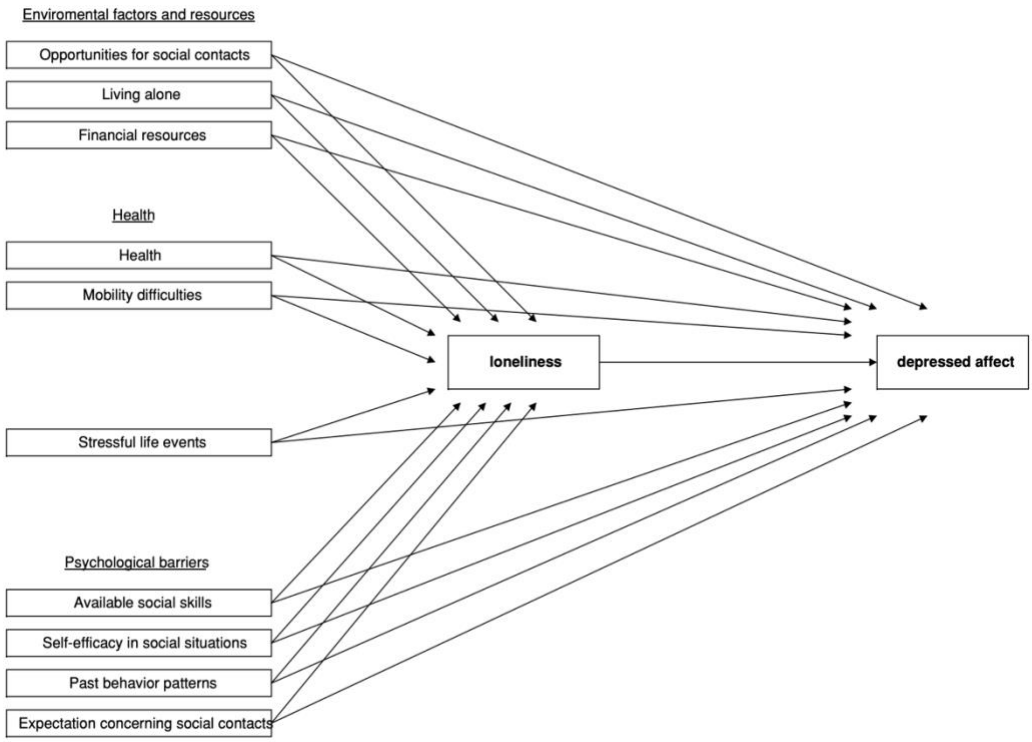


Figure 4. 2 The MODEL loneliness model

Adapted from *"Loneliness in older persons: a theoretical model and empirical findings" Cohen-Mansfield and Parpura-Gill, 2007.*

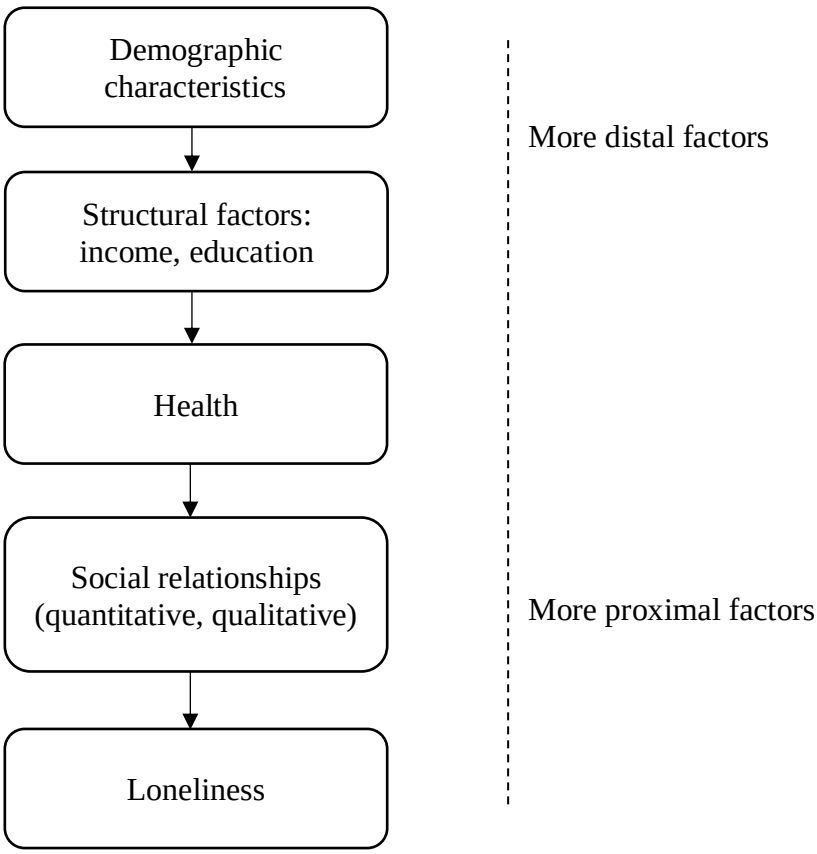


Figure 4. 3 The Filtration Model

Adapted from "From social structural factors to perceptions of relationship quality and loneliness: the Chicago health, aging, and social relationships study" Hawkley et al., 2008.

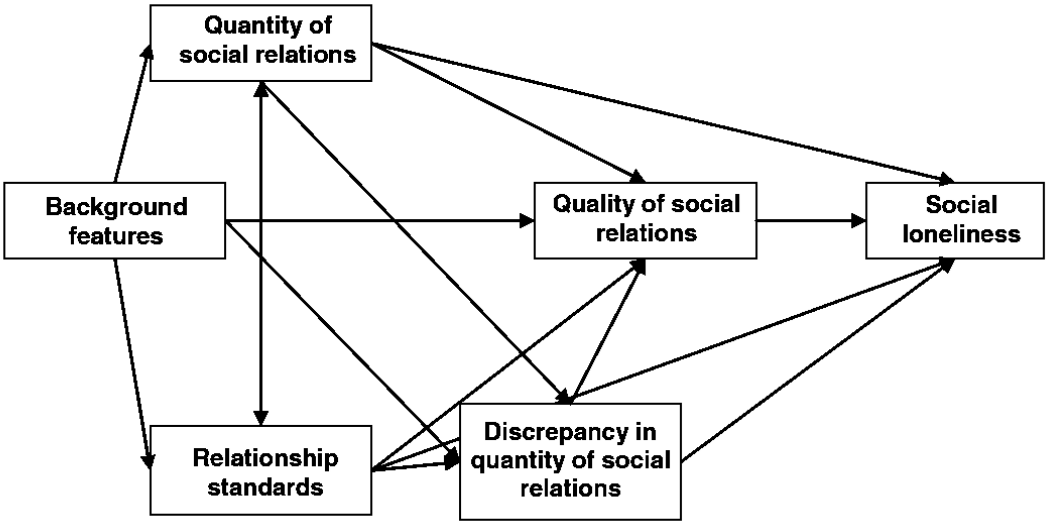


Figure 4. 4 The social relationship orientated model

Adapted from "The older, the lonelier? Risk factors for social loneliness in old age" Heylen, 2010

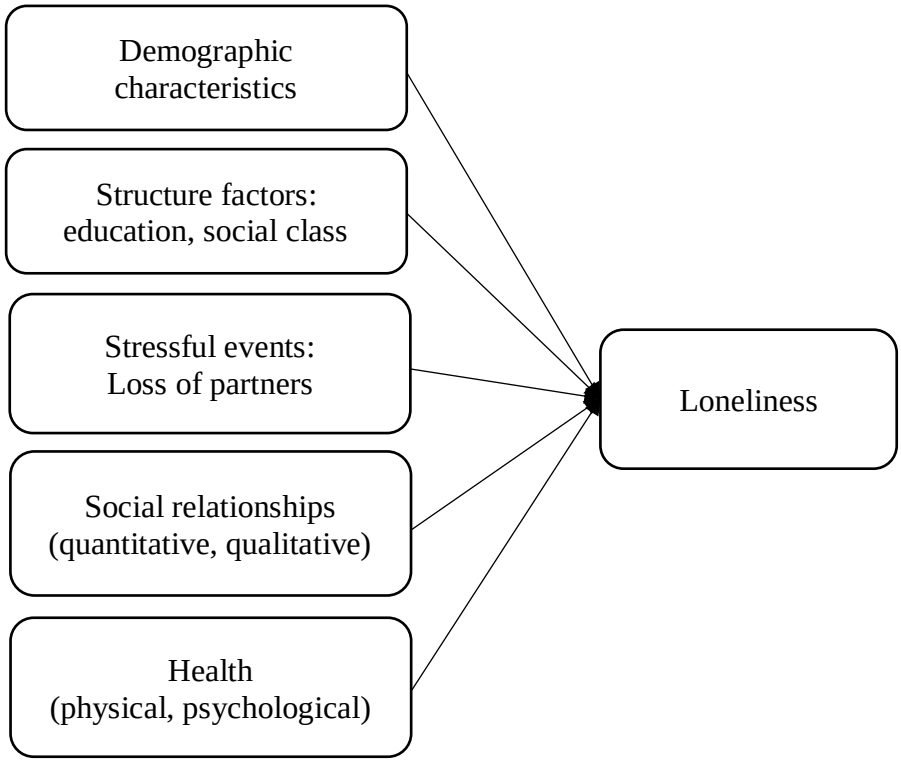


Figure 4. 5 The direct model

Furthermore, as stated in Chapter 1, most evidence is based on general older adults (aged 65 or over) with the oldest old (aged 80 or over) under-represented. Moreover, the life experiences of the young old differ from those of the oldest old. When the young old reach a very extreme age, they are more likely to be challenged with physical, mental and social changes.

Additionally, only a few studies have examined the associations between potential risk factors and loneliness changes over time. Of the studies that investigated the factors related to loneliness changes, most focused on loneliness onset instead of changes among different levels of loneliness (i.e. loneliness transition). To date, only one published study has explored risk factors for loneliness transition, and it is based on a relatively young old population (mean age 67 years) living in US (Hawkley and Kocherginsky, 2017). Again, highlighting the need to understand loneliness in the oldest old.

Chapter 1 has reported evidence of the association between loneliness and morbidity as well as between loneliness and mortality based on previous studies. Given the evidence to date on poor health associated with loneliness, potentially modifiable risks, and the lack of evidence on loneliness in the oldest old, this chapter first presents the scale of loneliness in the CC75C population, examines potential risk factors of loneliness, how loneliness changes in the same population measured over time, and identifies factors related to the changes observed.

4.3 Methods

4.3.1 Participants

Due to the availability of relevant variables, the analyses in this chapter focus on participants who attended wave 3 to wave 5 of the CC75C study. Detailed information about the study's design and sampling methods was presented in Chapter 3. An overview of data usage for this study is shown in Figure 4.6.

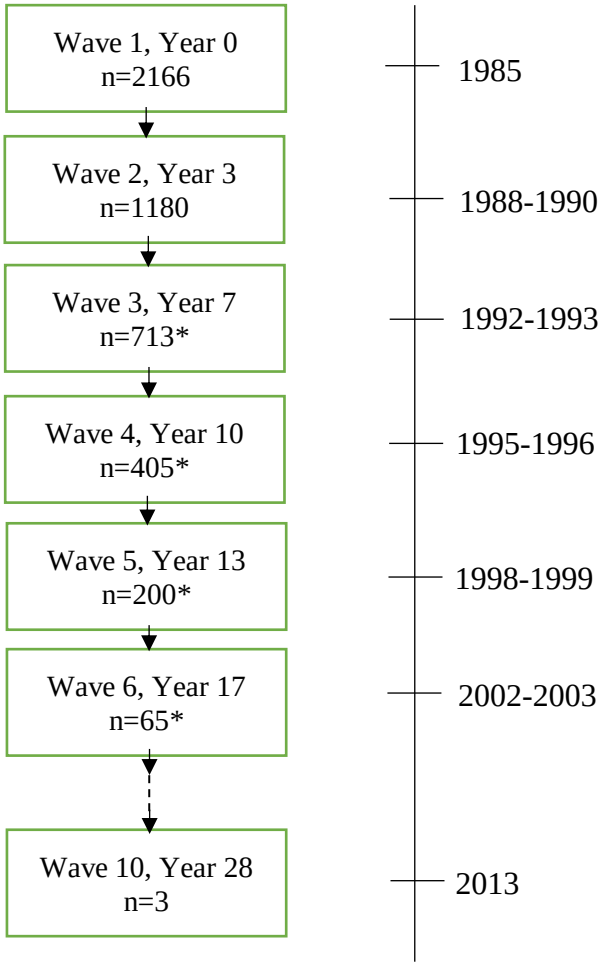


Figure 4. 6 Overview of data usage for the analysis of risk factors of loneliness
* indicates the number of eligible participants for current study.

4.3.2 Measures

Loneliness (described in Chapter 3) was used as the outcome variable, with socio-demographic characteristics, social contacts and health problems as potential risk factors. Loneliness was measured at each wave from wave 3 to wave 5, while all the other measures were recorded at wave 3.

Socio-demographic characteristics were age, sex, marital status (married, widowed, divorced/separated, single), length of widowhood (not widowed, 1-year widowhood, over 1-year widowhood), living arrangements, education and social class. Living arrangements consisted of living alone (hereafter refers to living without family members) and living with family members, e.g. spouse, siblings, children, in-laws and grandchildren. As participants who were institutionalised were unlikely to be living with family members, they were also categorised as living alone. Therefore, participants who were categorised as living alone included those who were living alone in community and those who were living in institutions.

Social contacts consisted of quantitative and qualitative perspectives. The quantitative aspect included the frequency of family contact and neighbour contact (never, less often, at least monthly, at least weekly, 2-3 times a week, and daily), as well as whether participants engaged in any social activities (over 60s' club, other social club, church, church group, voluntary work, other). In analysis, answers for frequency of family and neighbour contacts were divided into weekly to none and at least 2-3 times a week; the dichotomisation was made for the ease of statistical analysis, e.g. there were similar number of participants in weekly to none and at least 2-3 times a week categories (Appendix 4.1); answers for participations in social activities were recoded as 'no' if participants did not attend any of those activities and 'yes' if they engaged in at least one activity. The qualitative aspect referred to reported attitudes towards social contacts (i.e. family and friends contact: satisfied, not satisfied would like more contact, not satisfied would like less contact, and were further dichotomized into satisfied and unsatisfied), and whether participants went out as much as they wished (yes, no).

Health problems included self-rated physical health compared to peers (very good, good, fair, poor, and very poor. In analysis, answers were divided into three levels: very good, good, fair to poor), sight problems (no, yes), hearing problems (no, yes), depression and physical functioning.

4.3.3 Statistical analysis

A descriptive analysis was performed to provide prevalence of loneliness, then exploring in greater detail the distribution of individual-level factors according to loneliness level measured at wave 3. In analysis examining the associations between risk factors and loneliness, as loneliness was coded as an ordinal response, a proportional odds model was considered. However, the Brant test indicated that the proportional assumption did not hold. Therefore, the partial proportional odds model was used in analysis. Two models, univariable and multivariable analyses, were conducted. In multivariable analyses, two variables, marital status and social class, were excluded from analysis to avoid redundancy. For example, the variable length of widowhood was derived from the variable marital status (length of widowhood had three levels: not widowed, 1-year widowhood and over 1-year widowhood of which not widowed consisted of married, divorced/separated and single of variable marital status, and 1-year and over 1-year widowhood were derived from widowed status of marital status); and individuals who left school after 15 years were more likely to be in non-manual social class. Nevertheless, a sensitivity analysis was conducted including both education and social class, and results from this analysis did not differ substantially from results from analysis that excluded social class (Appendix 4.2).

To identify how experience of loneliness changes over a 7-year follow-up, data from three waves (wave 3 to wave 5) were used. To be included in analysis, participants had to answer the loneliness questions at all three waves. The typology of changing patterns of loneliness was adapted from previous studies (Victor and Bowling, 2012; Wenger and Burholt, 2004), where it consisted of ‘consistently non-lonely (remained non-lonely in all three waves)’, ‘consistently lonely (remained slightly or lonely in all three waves)’, ‘increased loneliness (became lonelier at later waves than at previous wave, including different combinations, such as non-lonely at wave 3, slightly lonely at wave 4, and lonely at wave 5; or slightly lonely at wave 3, lonely at wave 4 and 5)’,

‘decreased loneliness (became less lonely at later waves than at previous wave, also including different combinations, e.g. lonely at wave 3, slightly lonely at wave 4, and non-lonely at wave 5; or lonely at wave 3 and 4, slightly lonely at wave 5)’ and ‘fluctuated loneliness (the degree of loneliness at three waves was different and non-linear, e.g. non-lonely at wave 3, lonely at wave 4 and became non-lonely at wave 5)’.

To examine what factors are related to loneliness transitions over a 7-year follow-up, a multi-state model was used. Participants who had at least two waves’ data on loneliness (one wave must be wave 3) were included. Amongst eligible participants, those with missing data on risk factors were also excluded. In terms of model building, four states were constructed in this analysis. State 1, 2 and 3 indicated non-lonely, slightly lonely and lonely status, respectively. Death was treated as an absorbing state and labelled as state 4. Transitions among different states of loneliness and from different states of loneliness to death were permitted. Individuals who were lost to follow-up and known alive by the time wave 5 ended were accounted for by using censoring method. For estimation, transition was modelled on age (as a time-varying variable), sex and each potential risk factor, due to the limited information in the data that corresponded to certain transitions, categorical factors such as physical functioning and depression were treated as continuous variables with higher levels indicating greater limitations and depression. The process was run twice with different sets of initial values for the transition intensity to increase the robustness of estimation. Only factors that were significantly associated with loneliness transitions were reported. The goodness-of-fit test indicated the model was adequately fit.

4.3.4 Missing data

4.3.4.1 Missing data on loneliness

The total number of interviews for the wave 3 study was 713, of which 678 were conducted with participants (with/without their proxies), and the remaining 35 interviews were conducted with proxies because participants were unable or too impaired to participate in this study. 98% (665/678) of the participants responded to the loneliness item. For interviews conducted with proxies, participants’ loneliness was evaluated by proxies or interviewers. However, given loneliness was a subjective

term to describe the discrepancy between obtained social relationships and desired ones, participants' loneliness evaluated by participants' proxies or interviewers was regarded as missing. Missing loneliness item (i.e. loneliness item was not answered) was 7% of the responding participants on whom data were collected (48/713). Comparison analysis between participants who reported loneliness and those who did not showed that individuals who did not report loneliness were older and were more likely to be women, not married, living alone, left school before 15 years, in manual social class, having sight or hearing problems and having IADL and ADL disabilities. To adjust for this informative missingness on loneliness, inverse probability weighting was therefore used. The weighting process was modelled on age, sex, marital status, living arrangement, education, social class and physical functioning.

4.3.4.2 Missing data on risk factors

Regarding missingness on risk factors, 524 (79%) participants did not have missing values, and of the rest most (n=90, 14%) had missing values on one covariate. For each missing variable, the largest missingness being perceived physical health (7.5%), followed by depression (6.7%). Individuals with missing data were more likely to be older, women, living alone, having weekly to no contacts with neighbours, having self-rated fair to poor physical health, having IADL and ADL disabilities and depression, and were less likely to go out as much as they would like compared to those who had complete data.

In order to adjust for the data, two scenarios were assumed: missing at random (MAR) and missing not at random (MNAR). Correspondingly, two types of sensitivity analyses were conducted. First, under the assumption of MAR, the missing covariates were imputed by using the multiple imputation chained equations approach (Azur et al., 2011). The imputation procedure was modelled on age, sex, living arrangement, frequency of neighbour contact, attitudes towards going out, self-rated physical health, physical functioning, depression and loneliness. Second, under the assumption of MNAR, extreme case analysis (worst case analysis) was conducted. Therefore, the entire analyses were run twice; first was analysis with imputed data, and second was worst case analysis. The estimates from the two analyses did not

differ from each other substantively (Appendix 4.3). The results reported here were from analyses with imputed data.

In addition, as data used in this study were drawn from wave 3, to account for the dropout from wave 1 to wave 3, cross-sectional weight was applied. Analyses examining the association between risk factors and loneliness and investigating the changing patterns of loneliness over 7 years were conducted in Stata v13.1 (StataCorp LP, College Station, TX, USA). Analysis identifying risk factors for loneliness transitions was implemented in "msm" package in R (Jackson, 2011). A p-value <0.05 was considered statistically significant.

4.4 Results

4.4.1 Participants characteristics

The distribution of participants' characteristics is reported in Table 4.1. Of 665 participants who reported their loneliness levels, most did not experience loneliness, about a quarter experienced loneliness and the rest reported feeling slightly lonely. Compared to those who were not lonely, individuals who reported feeling slightly lonely or lonely were more likely to be older, women, widowed, losing spouses in the past year, living alone, having weekly to no contacts with family members, unsatisfied with social contacts, not going out as much as they like, having sight problems, hearing problems, or IADL and ADL disabilities, and depression (Table 4.1).

Table 4. 1 Sample description by loneliness level at wave 3 (weight applied, %)

	Not lonely	**Slightly lonely**	**Lonely**	**Total**
	58.9	16.0	25.1	100
Age				
80-84	44.2	40.0	34.1	41.0
85+	55.8	60.0	65.9	59.0
Sex[***]				
Men	36.4	22.7	20.4	30.2
Women	63.6	77.3	79.6	69.8
Marital status[***]				
Married	34.5	7.7	6.9	23.3
Widowed	51.6	82.2	84.9	64.8
Divorced/separated	2.5	1.6	1.1	2.0
Single	11.5	8.5	7.1	9.9
Length of widowhood[***]				
Not widowed	48.5	17.8	15.1	35.2
1 year	15.7	26.9	35.1	22.4
Over 1 year	35.8	55.3	49.8	42.5
Living arrangement[***]				
Live with others	44.7	19.2	9.6	31.8
Live alone	55.3	80.9	90.4	68.2
Education				
Left school <15 years	68.3	55.8	65.2	65.5
Left school ≥15 years	31.7	44.2	34.8	34.5
Social class				
Manual	63.5	49.8	58.9	60.1
Non-manual	36.6	50.2	41.1	39.9

Table 4.1 cont. Sample description by loneliness level at wave 3 (weight applied, %)

	Not lonely	**Slightly lonely**	**Lonely**	**Total**
	58.9	16.0	25.1	100
Frequency of family contact*				
At least 2-3 times a week	52.0	48.6	39.0	48.2
Weekly to none	48.0	51.4	61.0	51.8
Frequency of neighbour contact				
At least 2-3 times a week	57.9	46.6	52.0	54.7
Weekly to none	42.1	53.5	48.0	45.3
Quality of social contact***				
Satisfied with social contact	86.8	66.1	59.5	76.8
Unsatisfied with social contact	13.2	33.9	40.5	23.2
Social engagement				
No	52.4	55.3	61.0	55.0
Yes	47.6	44.7	39.0	45.0
Went out as like***				
No	34.8	49.6	63.5	44.3
Yes	65.2	50.4	36.5	55.7
Self-rated physical health				
Very good	30.7	33.9	29.2	30.9
Good	48.4	37.2	45.6	45.8
Fair to poor	20.9	28.9	25.2	23.3
Sight problems***				
No	65.1	53.0	43.0	57.9
Yes	34.9	47.0	57.0	42.1
Hearing problems**				
No	70.8	61.7	53.6	65.2
Yes	29.3	38.3	46.5	34.8
Physical functioning*				
None disability	34.3	39.9	33.3	35.0
IADL disability	30.2	19.7	19.3	25.9
IADL and ADL disabilities	35.5	40.4	47.4	39.2
Depression***				
No	94.6	81.4	72.6	87.2
Yes	5.4	18.6	27.4	12.8

Note: *** p<.001, ** p<.01, * p<.05 from chi-2 tests

4.4.2 The association between risk factors and loneliness

Advanced age and being a woman were significantly associated with loneliness in univariable analysis (Table 4.2), but the associations disappeared after taking other factors into account (Table 4.3). Widowhood had the strongest association with loneliness. Compared to individuals who were married, those who were widowed had a nearly 8-fold greater risk of reporting loneliness. Among individuals who were widowed, those who were recently widowed (lost spouses in the past year) had greater risk than those who were widowed more than one year (OR 6.1, 95% CI 3.8, 9.7 and OR 4.2, 95% CI 2.7, 6.3, respectively). As expected, the associations between length of widowhood and loneliness were attenuated after controlling for other factors (OR 4.2, 95% CI 2.2, 7.7 for recent widowhood and OR 2.4, 95% CI 1.4, 4.3 for more than 1-year widowhood, respectively). Compared to married people, being single (never married) was also significantly associated with loneliness, with an effect size only half that of being widowed. Compared to those who were living with others, living alone was associated with a 5-fold greater risk of loneliness with the association attenuated after adjustment. For social contacts, individuals who contacted their families less frequently had a 50% increased risk of reporting loneliness, a relationship which disappeared after full-adjustment. The associations with quality of social contacts were much stronger than frequency of social contacts; individuals who were unsatisfied with social contact were at four times greater risk of reporting loneliness, and those who did not go out as much as they would like were three times more likely to report loneliness. Although the associations were attenuated after controlling for other variables, the effects were still significant. However, neither the frequency of neighbour contacts nor the frequency of social engagements were found to be associated with loneliness. Having sight or hearing problems was associated with twice the risk of loneliness and although the associations were attenuated after controlling for other variables, they remained significant. Depression was associated with a near 5-fold increased risk of loneliness even after controlling for other factors. No statistically significant associations were found for loneliness by education level, social class, self-rated physical health and physical functioning limitations in either univariable or multivariable analyses.

Table 4. 2 The relationship of loneliness with potential risk factors cross-sectionally - univariable analysis (weight applied)

	Univariable Analysis	
Risk factors	**OR**	**95% CI**
Age (85+)	**1.4**	**1.0 -1.9**
Women	**2.1**	**1.4 -3.0**
Widowed	**7.6**	**4.5 - 12.7**
Divorced/separated	2.5	0.7 - 8.5
Single	**3.2**	**1.6 - 6.4**
Length of widowhood (1 years)	**6.1**	**3.8 - 9.7**
Length of widowhood (over 1 years)	**4.2**	**2.7 - 6.3**
Live alone	**5.4**	**3.6 - 8.0**
Education (left school >=15 years)	1.2	0.9 - 1.7
Social class (non-manual)	1.3	0.9 - 1.8
Weekly to none contact with families	**1.5**	**1.1 - 2.1**
Weekly to none contact with neighbours	1.3	0.9 - 1.8
Unsatisfied with social contact	**3.6**	**2.5 - 5.3**
Lack of social engagement	1.3	0.9 - 1.9
Did not go out as much as like	**2.7**	**1.9 - 3.7**
Perceived good physical health	0.9	0.6 - 1.4
Perceived fair to poor physical health	1.2	0.8 - 1.8
Sight problems	**2.1**	**1.5 - 3.0**
Hearing problems	**1.9**	**1.3 - 2.6**
IADL disability	0.7	0.5 - 1.1
IADL and ADL disabilities	1.2	0.8 - 1.7
Depression	**4.8**	**2.9 - 7.9**

Note: (1) OR: odds ratio; 95% CI: 95% confidence interval; (2) reference groups by order: age (80-84), men, married, not widowed, live with others, education (left school <15 years), social class (manual), frequency of family contact (at least 2-3 times a week), frequency of neighbour contact (at least 2-3 times a week), feeling satisfied with social contact, engaged in at least one social activity, went out as much as like, perceived very good physical health, did not have sight problems, did not have hearing problems, not disabled and not depressed (3) since the effect sizes of (lonely, slightly lonely) vs. not lonely was same with lonely vs. (slightly lonely, not lonely) from partial proportional odds model, only one set was reported.

Table 4. 3 The relationship of loneliness with potential risk factors cross-sectionally - multivariable analysis (weight applied)

	Multivariable analyses			
	A		**B**	
Risk factors	**OR**	**95% CI**	**OR**	**95% CI**
Age (85+)	1.0	0.7 - 1.5	-	-
Women	1.0	0.6 - 1.6	-	-
Length of widowhood (1 years)	**4.2**	**2.2 - 7.7**	-	-
Length of widowhood (over 1 years)	**2.4**	**1.4 - 4.3**	-	-
Live alone	**3.6**	**2.1 - 6.1**	-	-
Education (left school ≥15 years)	1.2	0.8 - 1.8	-	-
Weekly to none contact with families	1.4	0.9 - 2.2	-	-
Weekly to none contact with neighbours	1.1	0.7 - 1.7	1.0	0.6 - 1.6
Unsatisfied with social contact	**2.6**	**1.6 - 4.0**	-	-
Lack of social engagement	1.2	0.8 - 1.8	-	-
Did not go out as much as like	**2.0**	**1.3 - 3.0**	-	-
Perceived good physical health	0.8	0.5 - 1.3	-	-
Perceived fair to poor physical health	0.9	0.5 - 1.6	-	-
Sight problems	**1.5**	**1.0 - 2.3**	-	-
Hearing problems	**1.5**	**1.1 - 2.3**	-	-
IADL disability	0.7	0.4 - 1.2	-	-
IADL and ADL disabilities	0.8	0.5 - 1.3	-	-
Depression	**4.3**	**2.3 - 7.9**	-	-

Note: (1) OR: odds ratio; 95% CI: 95% confidence interval; (2) reference groups by order: age (80-84), men, not widowed, live with others, education (left school <15 years), frequency of family contact (at least 2-3 times a week), frequency of neighbour contact (at least 2-3 times a week), feeling satisfied with social contact, engaged in at least one social activity, went out as much as like, perceived very good physical health, did not have sight problems, did not have hearing problems, not disabled and not depressed (2) A: (lonely, slightly lonely) vs. not lonely; B: lonely vs. (slightly lonely, not lonely); '-': indicates same effect size.

4.4.3 Changes in loneliness over time in the same population

Table 4.4 shows how loneliness changes in the cohort over time. Approximately 40% of participants did not feel lonely at any of the three waves. For those who experienced changes of loneliness level, most had increased loneliness. Approximately 18% experienced decreased loneliness, and an additional 12% experienced fluctuating loneliness.

Table 4. 4 The trends of loneliness changes over 7-year follow-up (%)

Trends of changes	Total
Consistently non-lonely	37.2
Consistently lonely	8.6
Increased loneliness	24.6
Decreased loneliness	17.9
Fluctuating loneliness	11.8

Men were less likely than women to report loneliness at any wave and more likely to report absence of loneliness on all three occasions (Figure 4.7).

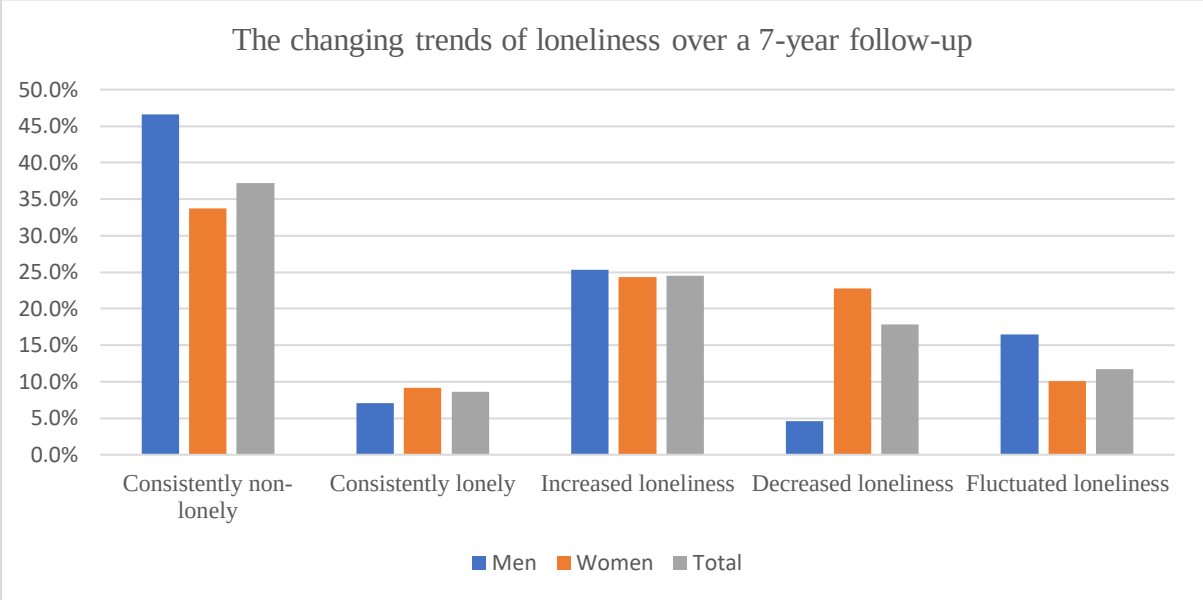


Figure 4. 7 Changes in loneliness during a 7-year follow-up by sex

4.4.4 Prediction of loneliness transition

Figure 4.8 & 4.9 show the relationships between risk factors and loneliness transitions. Higher physical functioning limitations and more severe depression were associated with 20% and 10% increased risk of transition from slightly lonely to lonely, respectively, and were negatively linked to recovery from lonely to slightly lonely status. Depression was also associated with increased risk of mortality from non-lonely state (HR 1.2, 95% CI 1.0, 1.4).

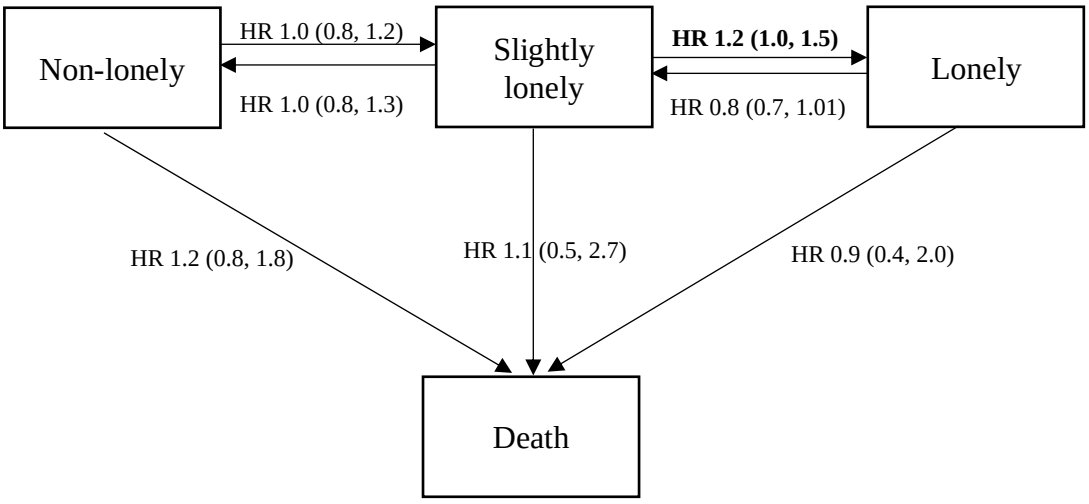


Figure 4. 8 Hazard ratio (HR) and 95% CI of physical functioning limitations on loneliness transition

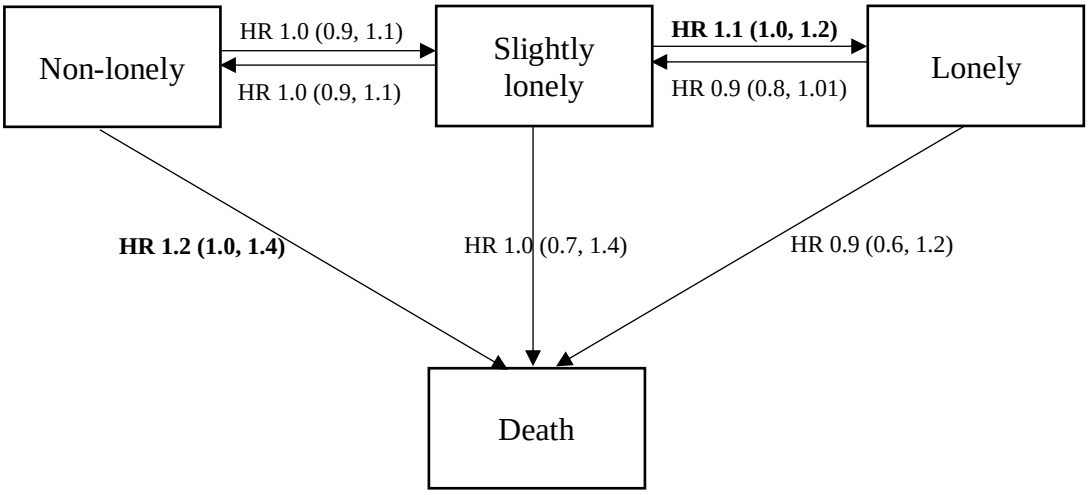


Figure 4. 9 Hazard ratio (HR) and 95% CI of depression on loneliness transition

4.5 Discussion

4.5.1 Main findings

Results from this study suggest that being widowed, living alone, being dissatisfied with social contacts, not getting out as much as the person would like, having sight or hearing problems and reporting depression were independently and significantly associated with increased risk of loneliness in the oldest old. The associations were more pronounced for loneliness among individuals who had been recently widowed. During the 7-year follow-up, over 60% of this very old population experienced loneliness at some point; the percentage of participants experiencing increased loneliness was greater than that experiencing decreased or fluctuating loneliness. Greater physical functioning limitations and more severe depression were found to accelerate the transition from slightly lonely to lonely.

4.5.2 Strengths and limitations

The current study draws data from one of the largest and longest-run population-based cohort studies of the very old. Data were collected through structured

interviews delivered by trained interviewers. Since data analysed in this study were from wave 3 and onwards, which was approximately seven years after the first wave, to adjust for dropout from wave 1 to wave 3, cross-sectional weight for wave 3 was computed. In addition, multiple imputation was used to account for missing data. Furthermore, to test whether those individuals reporting higher levels of loneliness were more likely to drop out during follow-up from wave 3 to wave 5, attrition analyses were conducted and the results showed that loneliness levels measured at the previous wave were not associated with subsequent dropout (Appendix 4.4). The current study includes a wide range of risk factors, which covers demographic characteristics, both quantitative and qualitative aspects of social contacts and social participation, physical health and depression.

There are a few limitations. The quantitative aspects of social contacts in the analysis did not consist of frequency of friend contacts; previous findings report that contact with friends may be more enjoyable than spending time with family members because contacting friends is a matter of choice whereas contact with family members might be obligatory (Singh & Misra, 2009). Despite that, the previous findings indirectly emphasise the importance of quality of social relationships in alleviating loneliness in old age; this is consistent with the findings from the current study. The direction of the associations between potential risk factors and loneliness cannot be tested in cross-sectional analyses. However, current findings provide areas to be tested longitudinally to determine the direction of the relationships. The use of a single-item loneliness scale could underestimate the true prevalence of loneliness if individuals feel admitting loneliness is socially undesirable. However, previous studies have found that single-item assessment is more appropriate for large surveys than other measurements and is well accepted by older people (Victor et al., 2005a). Physical functioning limitation was defined by ADLs and IADLs of which IADLs were measured through cooking and housework, it was possible that gender differences exist as women were more likely to be responsible for cooking and housework than men. However, having disabilities was found not to be related with loneliness in either univariable or multivariable analyses, therefore, it should not affect the overall conclusion of analyses of risk factors and loneliness; moreover, as the current study focused on exploration of risk factors of loneliness in population, gender differences in response to IADLs were unlikely to change the direction of the association of

physical functioning limitation and loneliness transition in multi-state modelling. Due to the limited number of men, sub-group analyses on gender were underpowered and were therefore not pursued. The associations between changes of risk factors such as changes of marital status and loneliness were not further explored as these data were not available. Such an analysis could explore strengthening or weakening of the effect of risk factors on loneliness. However, given the significant association between widowhood and loneliness, recent changes in marital status were unlikely to change the direction of overall association.

4.5.3 Interpretation of findings

In line with previous studies, this study found associations between marital status, living arrangements, the way that social contacts are perceived and social participation, health problems, depression and loneliness (Tijhuis et al., 1999; Jylha, 2004; Dykstra et al., 2005; Victor et al., 2005b; Lotfi et al., 2009; Dahlberg et al., 2015; Hawkley and Kocherginsky, 2017). This analysis revealed that the shorter the time interval after losing a spouse, the greater the risk of loneliness; this finding is supported by another loneliness study of the oldest old (Brittain et al., 2017). The mechanisms underlying such a graduated association are unclear, but it could be linked to the development of coping skills and resilience over time. It is also possible that individuals who lost spouses some time ago have built or re-built strong and satisfying connections with other family members or friends through which they obtain social support that protects against experiencing loneliness.

Consistent with previous studies, the result from the current study with the oldest old suggests that the experiences of loneliness change over time. Data drawn from previous studies with a young-old population suggest a rate of increased loneliness ranging from 11% to 25%, whereas the rate of recovery from loneliness ranges from 7% to 19%, about 40% to 50% remained non-lonely, 13% to 22% remained lonely, and approximately 12% experienced fluctuating loneliness over 3 to 20 years' follow-up periods (Jylha, 2004; Victor and Bowling, 2012; Brittain et al., 2017; Hawkley and Kocherginsky, 2017). The rate for each loneliness changing pattern in this study lay between the range of corresponding category shown from above studies, this study therefore broadly suggested that there was no difference on changing trend of loneliness between young-old and the oldest old.

Previous studies have reported mixed results for the relationship between depression and loneliness; moreover, MODEL suggested that the relationship between loneliness and depression might be the precursor of a vicious cycle, in which depression can be associated with physical inactivity, poor quality of social relationships, social disconnection, resulting in increased risk of loneliness and then further mood deterioration (Cohen-Mansfield and Parpura-Gill, 2007). The result from current analyses suggests that depression predicts loneliness transition from slightly lonely

status to lonely status over time, which indirectly supports the possibility that depression is a predictor of loneliness, not the other way around. Regarding the impact of physical functioning on loneliness transitions with increased transition from slight to manifest loneliness, the results support earlier research based on a much younger population which found that problems with physical function predicted loneliness over a 5-year period (Hawkley and Kocherginsky, 2017). Unlike the same earlier study in which cross-sectionally significant associations were reported with limited physical functioning and loneliness, this was not supported in the current study, suggesting the association between limited physical functioning and loneliness in the oldest old might be explained by other factors, such as widowhood. On the other hand, the significant association between physical functioning limitations and loneliness deterioration over a 7-year follow-up might be a reflection of the stress deterioration hypothesis, that is, the decreased physical functioning abilities limit individuals' capacity to obtain or maintain their social interactions, therefore putting them at risk of losing social connections and lacking social support (Warner and Adams, 2016), which in turn increases the risk of loneliness. The strong association between widowhood and loneliness in cross-sectional analysis is at odds with the fact that neither widowhood nor the length of widowhood was found to predict loneliness transitions over time after adjusting for age and sex. This finding seems paradoxical and could suggest that as time passes, individuals who lost spouses are able to develop coping skills to overcome the bereavement. Another possible explanation is that people tend to tune their expectations to their actual situation, and lowering expectations is one way to combat loneliness (Heylen, 2010).

4.6 Conclusion

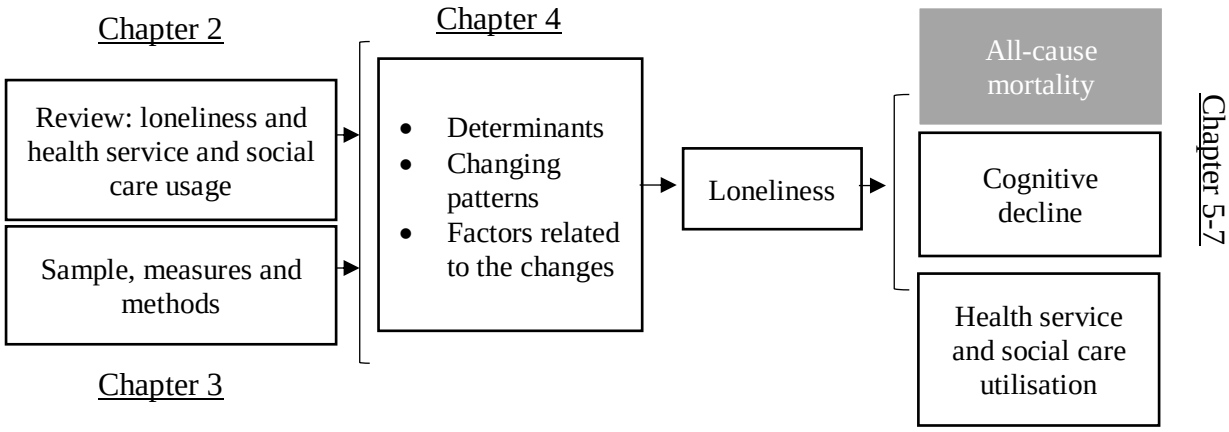
In this chapter, by using data from wave 3 to wave 5 of the CC75C study, the associations between individual-level factors and loneliness, changing loneliness in the oldest old over time, as well as the potential factors related to loneliness transitions, were explored. The results revealed that widowhood, especially the shorter length of widowhood, poor quality of social contacts instead of the low frequency of social contacts, having sight or hearing problems and depression were significantly associated with loneliness.

This study extended previous evidence by further examining potential factors related to loneliness transitions over a 7-year period. Greater levels of physical limitations and more severe depression were found to be associated with increasing loneliness. This finding is important as it could shed lights on future intervention developments. The correlates and potential determinants of loneliness, its changing patterns over time, as well as the association between predictor variables and loneliness transitions were investigated in this chapter. The following chapters will focus on investigating the influence of loneliness on health-related outcomes. The next chapter will examine the association between loneliness and all-cause mortality in the oldest old.

Chapter 5 Mortality risk of loneliness over a 10-year follow-up

5.1 Chapter Overview

This chapter investigates the effect of loneliness on all-cause mortality in the oldest old by using data from wave 3 to wave 5 of the CC75C. Death certification was obtained from the United Kingdom Office of National Statistics. Survival time was computed based upon the time that wave 3 was initiated and a follow-up of 10 years.



5.2 Introduction

In recent years, there has been a growing interest in the association between loneliness and mortality among older adults (Holt-Lunstad et al., 2015) although findings have not been entirely consistent. Several population-based studies have found a strong association between loneliness and mortality (Holwerda et al., 2012; Penninx et al., 1997; Shiovitz-Ezra and Ayalon, 2010; Tilvis et al., 2011) although other studies have failed to replicate this. For instance, in the English Longitudinal Study of Ageing (ELSA), after following 6500 men and women (aged 52 and older) for over 7 years, researchers did not find that loneliness was associated with increased mortality risk (Steptoe et al., 2013). A study with 3-year follow-up of 2200 Japanese elders found that loneliness was associated with mortality, but not after adjustment for health conditions (Sugisawa et al., 1994).

In most studies to date loneliness has been measured at a single time point. However, results from Chapter 4 indicated that many individuals' experience of loneliness changes over time. Failing to consider loneliness as a time-varying predictor limits our ability to better understand the nature of association between loneliness and mortality. To date, only one published study (focusing on men only, age range 64-84 years) has looked at the association between loneliness and mortality in which loneliness was treated as a time-varying factor. In that study, loneliness was assessed at four time points, and the association between loneliness and all-cause mortality and cardiovascular-related mortality did not reach statistical significance once sociodemographic characteristics and cardiovascular risk factors were taken into account (Julsing et al., 2016). The relationship between loneliness and mortality in the oldest old has only been explored in one study in which depression with loneliness lead to a doubled risk of mortality compared to depression alone (Stek et al., 2005).

5.3 Methods

5.3.1 Participants

This chapter's analysis was based on data drawn from wave 3, 4 and 5 of CC75C study as described in Chapter 3.

5.3.2 Measures

The choice of covariates was based on previous studies (Shiovitz-Ezra and Ayalon, 2010; Sugisawa et al., 1994). All covariates of interest were measured at wave 3. Demographic variables included age, sex, residential type (house/flat/granny flat, warden controlled house, council or private residential home, and long stay hospital), marital status and education. Co-morbidity was measured as the number of reported doctor-diagnosed chronic diseases, depression and physical functioning (described in Chapter 3).

All participants were flagged at the United Kingdom Office of National Statistics from where the death certification was obtained. The survival time for current analysis was computed based upon the time that wave 3 was initiated and a follow-up of 10 years. An overview of the analysis is presented in Figure 5.1.

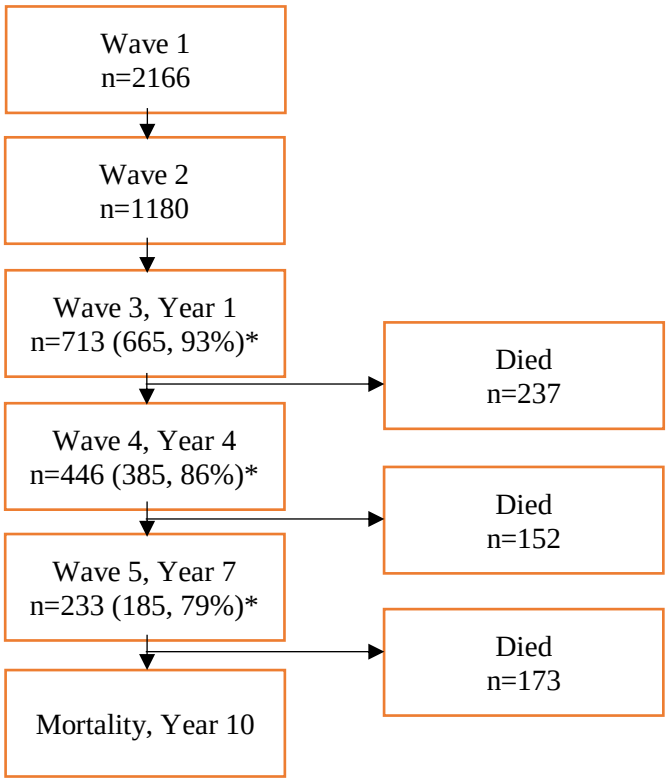


Figure 5. 1 Overview of data used for the analysis of the association between loneliness and all-cause mortality

* indicates the number and percentage of participants who reported loneliness level at each wave.

5.3.3 Statistical analysis

Only those participants with complete responses to the loneliness question at wave 3 (n=665) was included. A small number of individuals did not provide data on loneliness at wave 3 (n=48), to adjust for loneliness non-response, inverse probability weighting was included in the analysis as described in Chapter 4.

The participants' characteristics were firstly compared according to the level of loneliness measured at wave 3. The association between time-varying loneliness and all-cause mortality was investigated by using the Cox regression model with progressive adjustments for covariates. In total, three models were fitted: Model 1 was adjusted for age, sex and other demographic factors including residential type, marital status and education, Model 2 was further adjusted for number of doctor-

diagnosed diseases and physical functioning, and Model 3 was additionally adjusted for depression. The progressive adjustments were used to see how the association between loneliness and all-cause mortality is explained by covariates.

5.3.4 Missing data

In total, 162 participants reported their loneliness levels at all three waves, 354 reported loneliness data at wave 3 and wave 4 interviews, and 7 reported loneliness data at wave 3 and wave 5 interviews (Table 5.1). Detailed information on the number of participants at each wave, and the number of participants who reported their loneliness levels at each wave, is described in Appendix 5.1.

As the percentage of missing data on loneliness was relatively high (Appendix 5.1), excluding missing data may result in a biased conclusion. Missingness of loneliness at wave 4 and 5 was related to cognitive function measured at wave 3 (Appendix 5.2), suggesting a missing at random (MAR) analysis would address the bias (Little and Rubin, 2002). Thus, multiple imputation by chained equations was implemented to impute missing values on loneliness. The covariates included in the imputation model were those included in the Cox regression model with the addition of further variables: cognition, a status indicator (died or censored), time to death and number of waves the participants attended (Azur et al., 2011; De Silva et al, 2017; White et al., 2011). 30 sets were added in multiple imputation to obtain 30 sets of imputed data.

Table 5. 1 Summary of number of participants who reported loneliness level at each wave

Wave 3	Wave 4	Wave 5	Participants (n)
√	√	√	162
√	√	.	354
√	.	√	7

Note: '√' indicates reporting data on loneliness; '.' indicates missing data on loneliness.

5.3.5 Sensitivity analysis

Three sensitivity analyses were conducted. The first analysis aimed to test whether the association between loneliness and mortality was influenced by the length of follow-up. To do so, a 5-year mortality risk of loneliness was examined. The second analysis was to examine the possibility that the association between loneliness and mortality was moderated through unmeasured fatal diseases, such as cancer, by excluding individuals who died within one year of loneliness initially being recorded. The third analysis was to test the potential bias due to left truncation (i.e. left truncation occurs when participants meet the entry criteria but remain unobservable until a period after the start of follow-up: in this study, loneliness was measured from wave 3 onwards, but it is possible that individuals may have experienced loneliness over many years before wave 3). Results of sensitivity analyses are provided in Appendices 5.3-5.5.

All analyses were conducted after applying cross-sectional weight for wave 3. A p-value <0.05 was considered statistically significant. Statistical tests were implemented in Stata v13.1 (StateCorp LP, College Station, TX, USA).

5.4 Results

5.4.1 Participant characteristics

As described in Chapter 4, at wave 3 the mean age of participants was 86 years old (age range: 81-103 years). Most were women, living in a house/flat/granny flat, widowed, had left school before age 15, with fewer than two reported doctor-diagnosed diseases, and were disabled but not depressed (Table 5.2). Table 5.3 shows the weighted percentage of participants in each category according to loneliness level measured at wave 3. Of 665 participants, over half (59%) did not feel lonely, 16% reported feeling slightly lonely and a quarter reported loneliness. Being women, widowed, having both IADL and ADL disabilities, and depressed were associated with loneliness.

Table 5. 2 Participants' characteristics at wave 3

	No. of Participants	% of Participants
	665	100
Age		
80-84	304	46
85+	361	54
Sex		
Men	207	31
Women	458	69
Residence		
House/flat/granny flat	526	79
Warden controlled	76	11
Residential home/hospital	63	10
Marital status		
Married	165	25
Widowed	418	63
Separated/divorced	15	2
Single	67	10
Education		
Left school < 15 years	421	63
Left school ≥ 15 years	243	37
Number of chronic diseases		
0-2	409	64
≥3	227	36
Physical functioning		
No disability	249	38
IADL disability only	176	27
IADL and ADL disability	231	35
Depression		
No	538	87
Yes	78	13

Table 5. 3 The distribution of characteristics according to loneliness level (measured at wave 3, weight applied)

	Not lonely	Slightly lonely	Lonely	
%	59	16	25	Chi-2 p-value
Age				
80-84	44	40	34	0.098
85+	56	60	66	
Sex				
Men	36	23	20	<.001
Women	64	77	80	
Residence				
House/flat/granny flat	75	79	70	0.606
Warden controlled	11	7	13	
Residential home/hospital	13	14	16	
Marital status				
Married	34	7	7	<.001
Widowed	52	82	85	
Separated/divorced	2	2	1	
Single	11	8	7	
Education				
Left school < 15 years	68	56	65	0.072
Left school ≥ 15 years	32	44	35	
Number of chronic diseases				
0-2	67	66	57	0.128
≥3	33	34	43	
Physical functioning				
No disability	34	40	33	<.05
IADL disability only	30	20	19	
IADL and ADL disability	36	40	47	
Depression				
No	95	81	73	<.001
Yes	5	19	27	

5.4.2 The association between loneliness and all-cause mortality

A total of 562 participants died over the 10-year follow-up. The Kaplan-Meier survival curves for participants who did not feel lonely and who felt slightly lonely or lonely are shown in Figure 5.2. Table 5.4 presents the adjusted hazard ratios associated with loneliness. After adjusting for age, sex and other socio-demographic factors, feeling lonely was associated with a 20% increase in mortality risk (Model 1). The hazard ratios were attenuated to 1.1 (95% CI: 0.9, 1.5) after additional adjustment for number of chronic diseases and functional impairments (Model 2). The hazard ratios dropped to 1.0 (95% CI: 0.8, 1.4) after additional adjustment for depression (Model 3). Individuals who felt slightly lonely did not have increased risk of mortality relative to the non-lonely group.

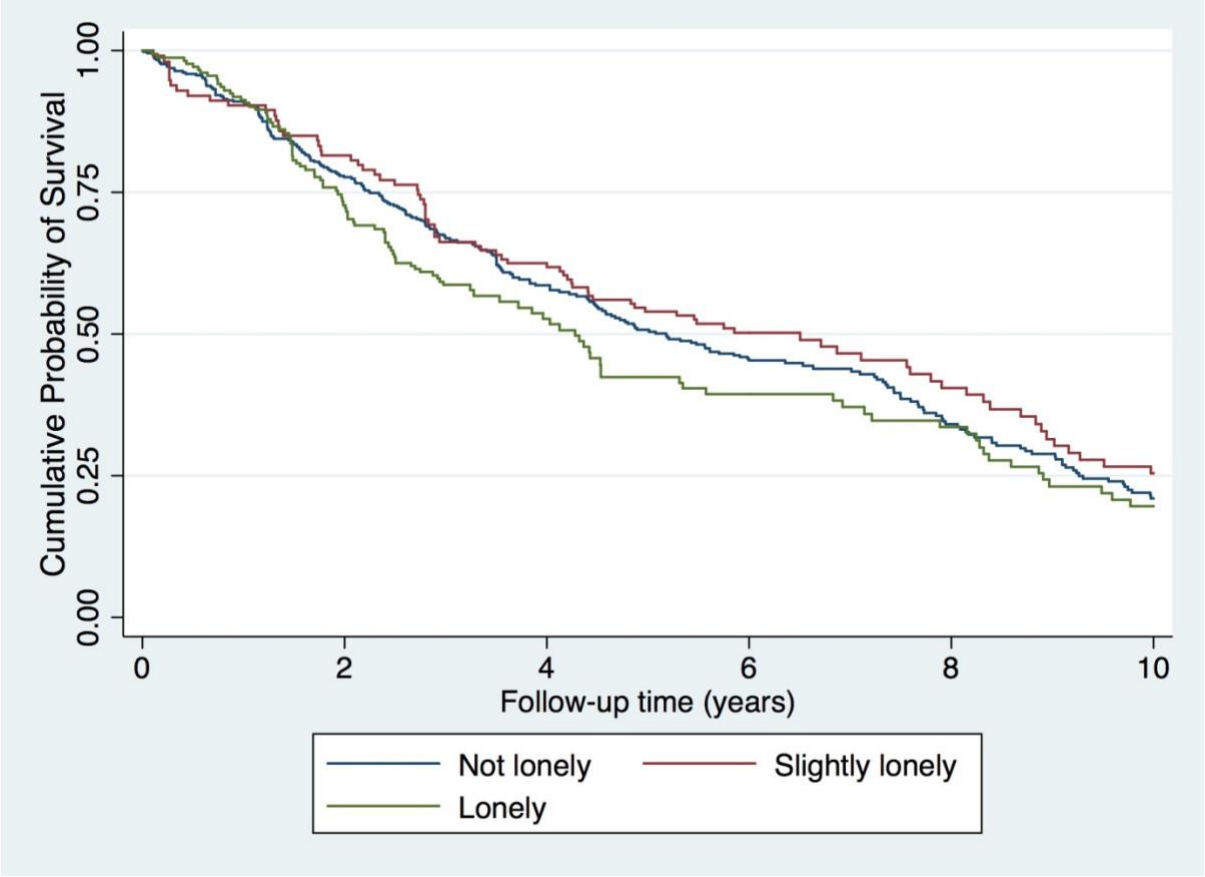


Figure 5. 2 The Kaplan-Meier survival curve

Results from the sensitivity analysis testing the effect of loneliness on 5-year mortality were generally in line with the results in the main analysis. The significance

of the association between loneliness and mortality remained after adjusting for socio-demographic factors and physical health (i.e. number of chronic diseases and functional impairments) but, as in the 10-year survival analysis, disappeared after further adjustment for depression (Appendix 5.3). In addition, the estimated hazard ratio excluding individuals who died in the first 24 months remained similar to the results in the main analysis (Appendix 5.4).

Table 5. 4 Mortality risk of loneliness

	Model 1		Model 2		Model 3	
	HR	95% CI	HR	95% CI	HR	95% CI
Not lonely	1.0	-	1.0	-	1.0	-
Slightly lonely	0.9	0.7 - 1.3	0.9	0.7 - 1.2	0.9	0.7 - 1.2
Lonely	1.2	1.0 - 1.6	1.1	0.9 - 1.5	1.0	0.8 - 1.4

Note: HR: hazard ratio, 95% CI: 95% confidence interval.

Model 1: adjusted for age, sex, residential type, marital status and education.

Model 2: Model 1 further adjusted for number of chronic diseases and physical functioning.

Model 3: Model 2 further adjusted for depression.

5.5 Discussion

5.5.1 Main findings

This chapter investigated the associations between loneliness and all-cause mortality in a very old population, using a relatively large sample. Feeling lonely was not associated with an increased risk of mortality in the oldest old over a 10-year follow-up after taking participants' co-morbidity into account. No association was found between slight loneliness and mortality. The results from sensitivity analyses suggested that the results from main analysis were not biased due to left truncation and the unmeasured fatal diseases did not moderate the association between loneliness and all-cause mortality for this study population. In addition, findings from analysis of 5-year mortality risk of loneliness suggested that mental health problems might have more direct effects on mortality risk than physical health decline at later life stages.

5.5.2 Strengths and limitations

This is the first study to investigate the association between loneliness and all-cause mortality in the oldest old. Strengths include multiple measures of loneliness during follow-up and inclusion of a wide range of covariates, which help to test the association between loneliness and all-cause mortality more thoroughly. In addition, the use of cross-sectional weight adjusting for dropout from wave 1 to wave 3 provides a way to address response biases.

One of the potential limitations is that the covariates in these analyses were measured at one time point. There is a possibility that changes in covariates during follow-up could contribute to subsequent changes in loneliness level (Tijhuis et al., 1999; Victor and Bowling, 2012). However, in the current analyses, the time-varying nature of loneliness has been taken into account. Despite changes in covariates possibly influencing the overall association, the conclusion from the current study was that loneliness was not associated with increased mortality risk. Covariates indicating co-morbidity – the number of doctor-diagnosed chronic diseases, physical functioning and depression – were self-reported rather than confirmed from medical records or diagnostic assessments, so are potentially either over- or under- reported. Although this study adjusted for a wide range of confounders, the possibility that the relationship between loneliness and mortality may be affected by other unmeasured factors cannot be completely ruled out. However, results from sensitivity analysis excluding individuals who died within one year were similar to the results from the main analysis, implying that terminal illness is not a key factor.

5.5.3 Interpretation of findings

The finding from this study that loneliness was not significantly associated with increased mortality risk after controlling for health problems is in line with previous studies with younger samples (Julsing et al., 2016; Steptoe et al., 2013; Sugisawa et al., 1994). Although in this study the specific mediation analysis that tests the causal mechanisms underpinning the association between loneliness and mortality was not conducted, the reduction in hazard ratio and the loss of significance in the association after adjusting for co-morbidity indicated that the association between loneliness and

all-cause mortality was fully explained by participants' health conditions. This is supported by a US population-based study with 2-year follow-up of a younger old population which reported that health status and self-rated health were the proximal mechanisms through which loneliness affected mortality risk. In particular, loneliness predicted increases in depressive symptoms and physical impairments and decreases in subject health, which in turn increased the risk of mortality (Luo et al., 2012). Apart from physical health, mental health may also play a mediation role in the association between loneliness and mortality. For example, the Longitudinal Aging Study Amsterdam (LASA) found that mortality risk of loneliness was only partially explained by physical health, but was fully explained with a further adjustment for mental health and cognitive function (Ellwardt et al., 2015).

Although the analysis excluding individuals who died in the first 12 months provided similar results to those in the main analysis, it is possible that loneliness is an early sign of undiagnosed diseases, raising a question of whether a reverse causation exists in which individuals with undiagnosed diseases are more likely to report feeling lonely. In addition, as stated earlier, loneliness may impact on mortality risk through multiple pathways, such as physiological pathway (e.g. chronic diseases, self-rated health) or psychological pathway (e.g. mental health, cognitive function) or both. Since many of the previous studies have focused on the physiological pathway, future research should pay more attention to testing the role of psychological factors, such as cognition, as the potential mediator for the association between loneliness and mortality.

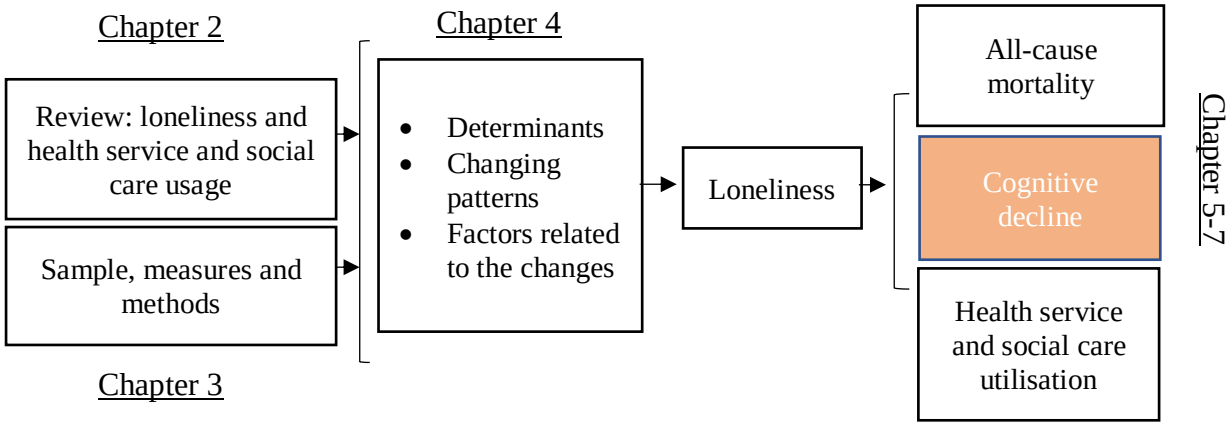
5.6 Conclusion

This chapter examined the impact of loneliness on all-cause mortality in the oldest old over a 10-year follow-up. The result showed that after controlling for health problems, loneliness was not a significant risk factor for mortality. In other words, loneliness is not a proximal risk factor for mortality. Health conditions have more direct effects on mortality than loneliness does. Health problems included in this chapter were physical health conditions and depression, whether cognitive decline plays a role in the association between loneliness and mortality in the oldest old remains unknown. In order to answer this question, the next chapter will focus on investigating the association between loneliness and cognition.

Chapter 6 Loneliness and cognitive decline over a 20-year follow-up

6.1 Chapter Overview

The association between loneliness and cognition was investigated using data from wave 3 to wave 10 of the CC75C study. The specific objectives of this chapter are (1) to examine the effect of baseline loneliness (measured at wave 3) on cognitive transition over a 20-year follow-up and (2) to investigate the effect of changes of loneliness on cognitive decline over a 20-year follow-up.



6.2 Introduction

The association between loneliness and all-cause mortality in the oldest old was investigated in Chapter 5. The results indicated that participants' physical health, including the number of self-reported doctor-diagnosed chronic diseases, physical functioning limitations and depression, explained the association between loneliness and mortality. However, apart from physical health, other factors, such as cognitive decline, have also been suggested to mediate the association between loneliness and all-cause mortality (Ellwardt et al., 2015). Previous studies examining the association between loneliness and cognitive decline have been almost exclusively based on the younger old. It is unclear whether there is an association between loneliness and cognitive function in the oldest old. To explore an additional potential pathway through which loneliness may exert effects on mortality and to answer the question of whether loneliness is related to cognitive decline in the oldest old, this chapter aims to investigate the association between loneliness and cognition by following participants over a 20-year period. The specific objectives include:

(1) To examine whether baseline loneliness (measured at wave 3) is associated with transitions in and out of different cognitive states.
(2) To investigate the association between changes of loneliness (time-varying risk factor) and cognitive decline.

6.3 Methods

6.3.1 Participants

For current analysis, participants were drawn from wave 3 to wave 10 of the CC75C study. Please see Chapter 3 for a detailed description of CC75C study.

6.3.2 Measures

Information on loneliness, cognitive function and other individual-level factors was reported in Chapter 3.

Briefly, in this analysis, loneliness was the primary risk factor; cognitive status was the outcome, it was assessed by MMSE and defined as: severe cognitive impairments (score 0-17), moderate cognitive impairments (score 18-21), mild cognitive impairments (score 22-25), and normal cognition (score 26-30); the categories moderate cognitive impairments and severe cognitive impairments were combined into one category, moderate/severe cognitive impairments, in subsequent analysis due to the small frequency; age, sex, and education were included as confounders. The choice of confounders was based on previous studies (Brayne et al., 1999; Dufouil et al., 2000; Matthews et al., 2012).

6.3.3 Statistical analysis

Two analyses were conducted. In the first analysis, the association between baseline loneliness (measured at wave 3) and cognitive transition was examined by using multi-state modelling. The model consisted of three living states: normal cognition, mild cognitive impairment (MCI) and moderate/severe cognitive impairments, and an absorbing state: death. Transitions from each living state to death were allowed. Forward transition from normal cognition to MCI, and from MCI to moderate/severe CI along with backward transition from MCI to normal cognition were also allowed. But recovery from moderate/severe CI to MCI was not allowed as such transition was rarely observed in clinical situation (Marioni et al., 2012). When such transition was observed, it was treated as misclassification. The transition intensities were modelled as a function of time (in years since wave 3), sex and loneliness. The model was run with two different sets of initial values to test the robustness of estimation.

In the second analysis, the association between changes of loneliness and cognitive decline was examined by using a population-averaged model: the generalized estimating equations (GEE) with an independent working correlation structure. The model was adjusted for MMSE nonresponse at wave 3, cohort effects (defined by age group at baseline: 80-84, 85-89 and 90+), time (in years since wave 3), sex, education, interaction term of time and sex, and interaction term of time and education. The GEE was run after applying cross-sectional weight for wave 3.

Multi-state modelling was performed using 'MSM' packaged in R (Jackson, 2011), and the GEE was conducted in STATA, version 13.1 (Stata Corp LP, College Station, Texas). A p-value of <.05 was considered statistically significant.

6.3.4 Missing data

At wave 3, of 713 participants, 657 had valid MMSE scores. MMSE measures were not available for participants whose only data were from proxy informant interviews (n=35), participants unable to complete all MMSE questions due to physical or sensory difficulties (n=3), and participants for whom all MMSE items were coded 'Not asked', 'Refusal' or 'Do not know' (n=18). Individuals who had invalid MMSE scores (i.e. individuals who had incomplete or no MMSE scores) were more likely to be older and disabled (measured through reported functional performance of daily activities) than those who had valid MMSE scores (Appendix 6.1). To adjust for MMSE non-response, inverse probability weighting was calculated based on age, sex and physical functioning.

During follow-up, a large number of participants were lost to the study through death and dropout (i.e. refused, moved away). It is already well known from this study's previous work on dropout (Fleming et al., 2007) and others that this feature of studies of the oldest old is highly related to many factors and is not missing at random. For this thesis, a dedicated analysis was conducted again. Results from logistic regression showed that the dropout at wave (t) was significantly related to age and MMSE score measured at previous wave (t-1) (Appendix 6.2), suggesting a missing not at random process (Little and Rubin, 2002). In addition, for individuals who remained in the study and provided a valid MMSE score, a few did not report loneliness (Appendix 6.3). Since the percentage of missing data on loneliness was relatively low among participants who had valid MMSE scores, multiple imputation by chained equations was performed to adjust for MMSE missingness only according to guidance on procedure for multiple imputation in longitudinal studies (Spratt et al., 2010). Sensitivity analysis adjusting for both MMSE and loneliness missingness was also conducted. As the aim of current analysis was to examine the influence of loneliness on cognitive function in the mortal cohort (Chapter 3), the imputed data were then

reset to be missing for deceased participants in waves after their death (Jones et al., 2015).

6.4 Results

6.4.1 Cohort and participant description

Table 6.1 presents a summary description of demographics, education level and reported loneliness for participants who were interviewed at each wave. It also summarises attrition between waves, as can be seen, mortality far outweighing other dropout for all waves. At wave 3, the mean age of participants was 86, and most were women. The percentage of women increased in each wave as the cohort aged until the surviving sample size was too small to detect any significant trend. Individuals who left school aged 15 or older were more likely to remain in the study. The proportion of participants who reported feeling slightly lonely or lonely fluctuated over time.

Table 6. 1 Description of participation and characteristics of participants at each specific wave

	W3	W4	W5	W6	W7	W8	W9	W10
Interviewed (n)	713	405	200	65	26	10	3	1
Died (n)		237	152	109	36	13	7	0
Dropped out (n)		71	53	26	3	3	0	2
Age (m, sd)	86.4 (4.0)	88.7 (3.7)	91.4 (3.0)	94.2 (2.3)	97.4 (1.5)	98.3 (1.3)	100.3 (0.6)	102.0 (na)
Women (%)	71.0	72.7	75.1	81.0	87.8	79.3	65.8	0
Left school ≥15 (%)	33.6	37.1	37.9	43.3	57.8	80.1	100.0	100.0
Slightly lonely (%)	16.2	26.1	25.0	17.1	40.4	11.0	0.0	100.0
Lonely (%)	24.7	16.4	20.1	33.7	6.6	33.4	0.0	0.0

Note: na: not applicable. Reference groups in order: men, left school < 15, not lonely.

The proportion of participants identified in each of the four MMSE groups is described by age group and gender in Figure 6.1. Lower MMSE scores were found for older age and women. At wave 3, about 28% of participants had moderate to severe cognitive impairments (MMSE ≤ 21) and an additional 28% had mild cognitive impairment (22≤MMSE≤25). The prevalence of cognitive impairments increased with age and was higher in women (MMSE ≤21: 32%; 22≤MMSE≤25: 31%) than men (MMSE≤21: 21%; 22≤MMSE≤25: 24%).

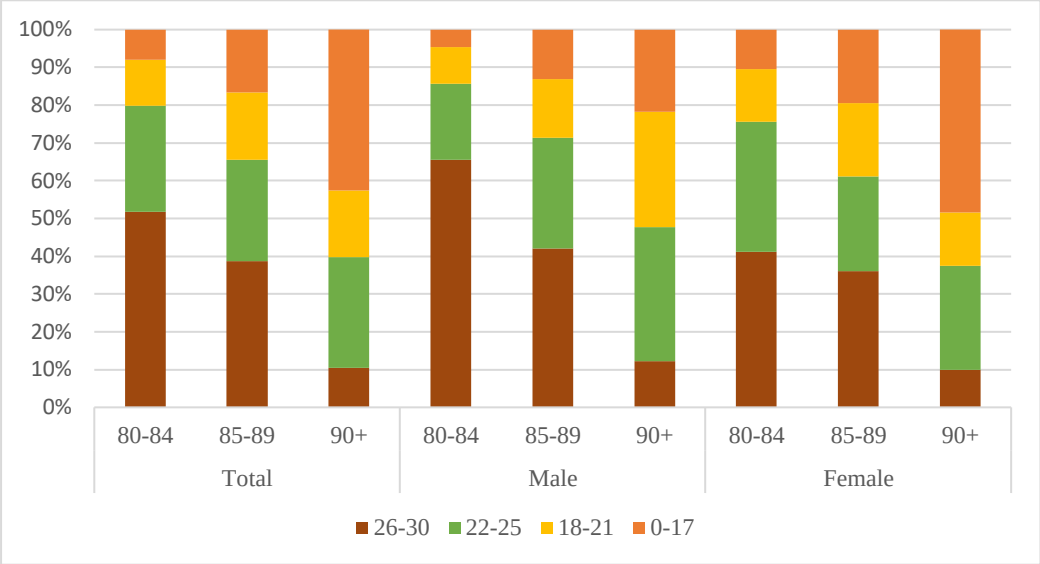


Figure 6. 1 Proportion of MMSE scores by age and gender

Note: the missingness of MMSE was adjusted by inverse probability weighting

The flow of participation according to the availability of MMSE is described in Figure 6.2. The participants whose MMSE scores were labelled as invalid MMSE scores at wave 4 and onwards were those who were interviewed but the MMSE was not done, those who were not interviewed in person but their proxy informants were, and those who had dropped out since the previous wave.

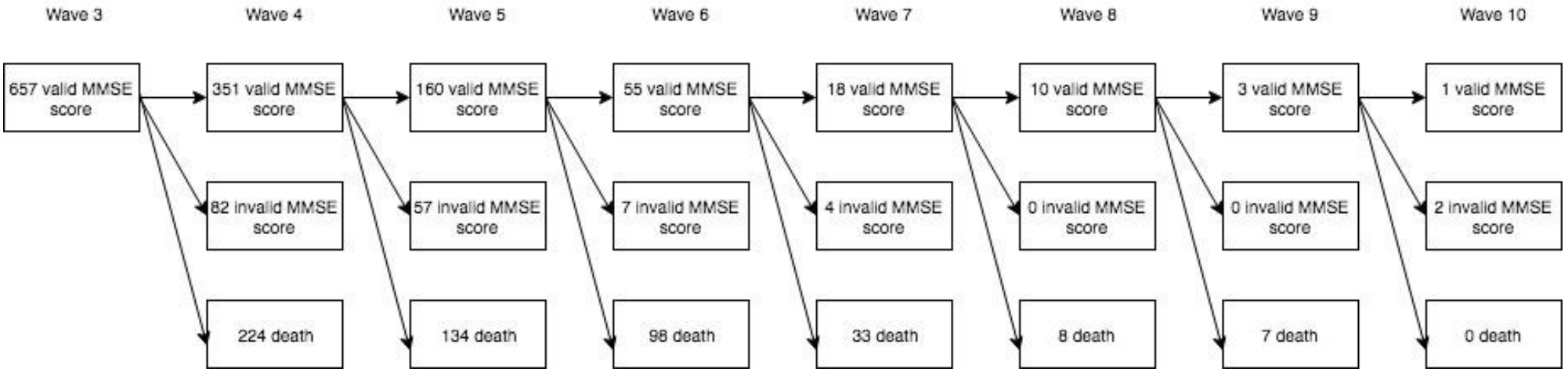


Figure 6. 2 Flow of MMSE availability at each wave

6.4.2 The effects of loneliness on cognitive changes

6.4.2.1 Baseline loneliness and cognitive transition

There was no evidence of an association between loneliness level measured at wave 3 and subsequent cognitive transitions (Figure 6.3, 6.4). Moreover, loneliness did not accelerate the transitions from different cognitive states to death.

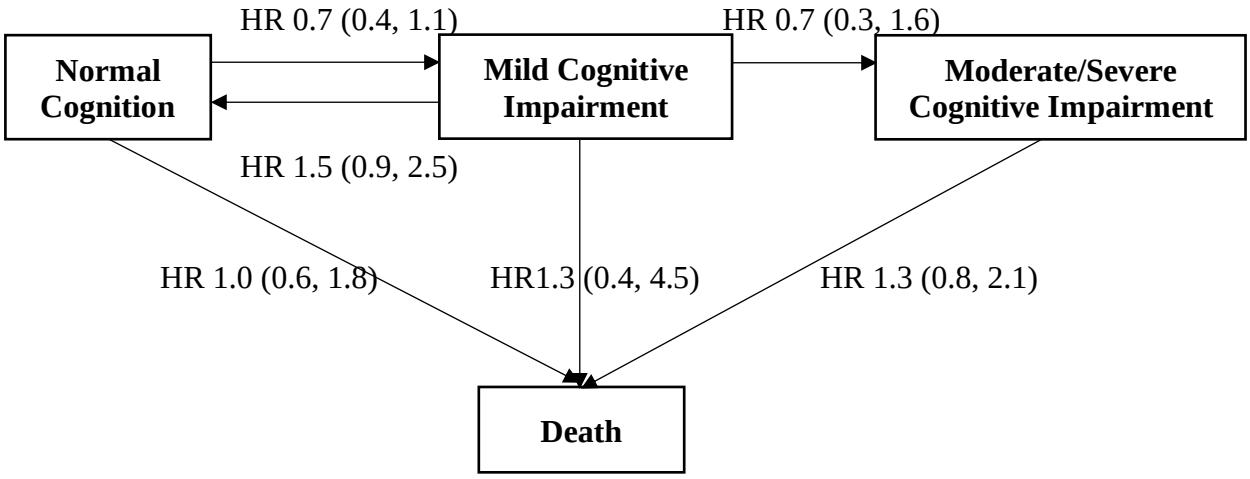


Figure 6. 3 Hazard ratios and 95% confidence intervals for cognitive transitions and death associated with feeling slightly lonely versus not feeling lonely
Note: HR: hazard ratio

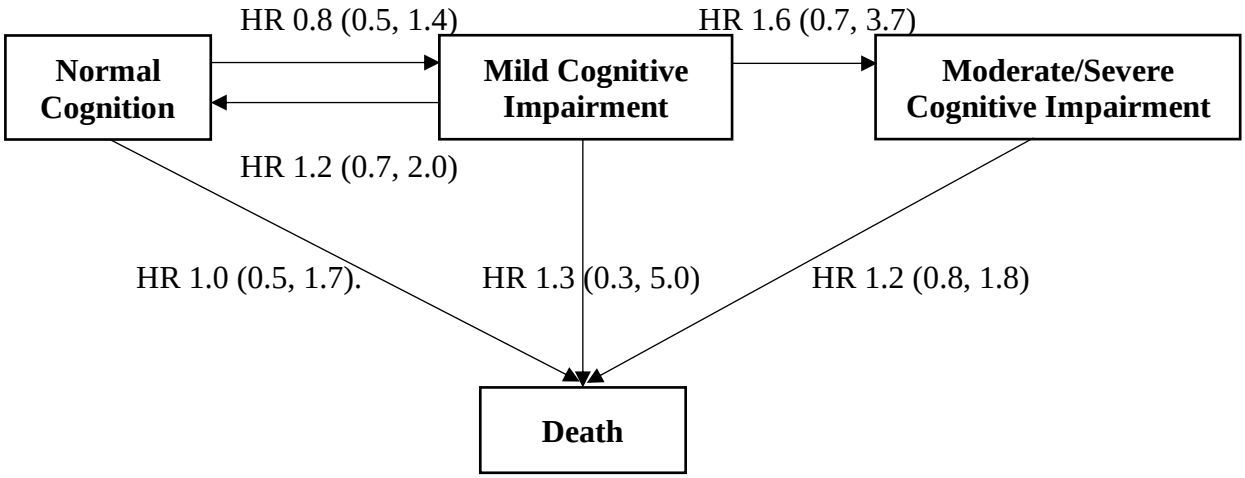


Figure 6. 4 Hazard ratios and 95% confidence intervals for cognitive transitions and death associated with feeling lonely versus not feeling lonely
Note: HR: hazard ratio

6.4.2.2 Time-varying loneliness and cognitive decline

Results from GEE modelling revealed that on average, feeling slightly lonely and lonely were both associated with decline in cognitive function, but neither of these associations was significant, whereas the associations with age, sex and years of education were all significant (Table 6.2). Compared with individuals who were aged 80-84 years, mean MMSE scores were lower by 1.3 and 5.3 points for those who were aged 85-89 and those who were aged 90 or older, respectively. On average, MMSE scores were about 1 point less for women than men; in addition, over time women had a faster average drop in MMSE than men. There was also a difference in mean MMSE scores between individuals who left school aged less than 15 years old and those who left school 15 or older; specifically, individuals who left school before they were 15 had a mean MMSE about 3 points lower than their counterparts (Table 6.2). Results from sensitivity analysis did not differ substantively from results in the main analysis (Appendix 6.4).

Table 6. 2 Results from GEE model estimating impact of time-varying loneliness on cognitive function decline

	Coefficient	95% CI
Loneliness level		
Slightly lonely	-0.6	(-1.7, 0.4)
Lonely	-0.6	(-1.5, 0.4)
Age		
85-89 (at wave 3)	-1.3	(-2.2, -0.5)
90+ (at wave 3)	-5.3	(-7.1, -3.5)
Time	0.6	(-0.8, 2.0)
Sex		
Women	-1.1	(-2.1, -0.1)
Women x Time	-0.9	(-1.8, 0.003)
Education		
Left school <15 years	-2.8	(-3.7, -1.8)
Left school <15 years x Time	0.2	(-0.7, 1.1)

Note: references groups: not lonely, aged 80-84 at wave 3, men, left school ≥15 years. Time: number of years since wave 3.

6.5 Discussion

6.5.1 Main findings

Results from the current study indicated that neither baseline loneliness nor time-varying loneliness were associated with cognitive decline among people at very late life stage.

6.5.2 Strengths and limitations

This is the first study to examine the association between loneliness and cognitive changes over time in the oldest old. The prospective cohort design confirms the direction of this relationship. In addition, the association between loneliness and cognition is examined thoroughly by using repeated measures of loneliness and cognition. Moreover, the use of cross-sectional weight and the weight adjusting for MMSE missingness at wave 3 can make the study sample as representative as the original study population. Furthermore, the use of multi-state modelling can accommodate some of the inherent challenges of such longitudinal studies including misclassification of cognition and dropout due to death.

There are a few limitations. Firstly, as with other longitudinal studies, a large amount of loss to follow-up was observed. The decreased number of participants can lead to a decrease in statistical power. However, multiple imputation avoided further sample size reduction which would otherwise have resulted from exclusions due to missing data. Secondly, although the logistic analyses showed that the dropout at each wave was associated with age and MMSE measured at the previous wave, we cannot rule out the possibility that missing data was missing not at random (MNAR). However, it has been reported that under mortal cohort scenario, multiple imputation can be used adequately when missing data is both missing at random (MAR) and missing not at random (MNAR) (Jones et al., 2015). Thirdly, previous studies have shown that social loneliness had a stronger association with MMSE than did emotional loneliness (Holmen et al., 2000). The different aspects of loneliness cannot be assessed by a single-item scale. Consequently, the association between social loneliness and emotional loneliness and cognition cannot be investigated. Finally, due to the availability of data, the effects of loneliness on specific cognitive domains cannot be examined; previous studies have reported inconsistent findings on the association between loneliness and cognitive domains. For instance, Wilson and colleagues found that loneliness was linked to reduced verbal memory and sematic memory, whereas, O'luanaigh et al. did not find such associations in their study (O'lunaigh et al., 2012; Wilson et al., 2007).

6.5.3 Interpretation of findings

Previous studies have reported conflicting results on the associations between loneliness and cognitive function based on a relatively young old population (DiNapoli et al., 2014; Gow et al., 2013; O'luanaigh et al., 2012; Yeh and Liu, 2003). The current study adds evidence to the literature that loneliness is not associated with cognitive decline in the oldest old. Therefore, it is unlikely that cognitive decline acts as a mediator in the association between loneliness and mortality for individuals at very old age.

One possible explanation for the inconsistency might be that many of the previous studies with young old population were using cross-sectional design (Boss et al.,

2015). There might be a reverse causation existing in the association between loneliness and cognitive impairments. Some researchers have argued that reduced social resources are an early sign of cognitive function decline (Barnes et al., 2004). It is possible that individuals who have impaired cognition are less likely to participate in social activities; consequently, they are at greater risk of feeling lonely.

Another possibility is that current study included participants as long as they had valid MMSE scores regardless of cognitive status (Figure 6.1). In studies which report a significant association between loneliness and cognitive decline, only participants with normal cognitive ability were included at baseline (O'luanaigh et al., 2012). It is possible that the weakened association between loneliness and cognitive decline in this analysis is due to the existing interactions between loneliness and cognitive impairments prior to the baseline. However, the non-significant association between loneliness and cognitive transition suggests that loneliness is not linked to cognitive changes, irrespective of cognitive status.

Interestingly, in a study conducted in Finland with 650 elders who were aged 75, 80 and 85 years at study entry (Tilvis et al., 2004), the cross-sectional relationship between loneliness and cognitive function was not supported, nor with cognitive decline during a 5-year follow-up. This study did, however, report a significant association between loneliness and cognitive decline at a 10-year follow-up. It is unclear whether the new emerged association between loneliness and cognitive decline reflects a threshold in "cognitive reserve theory" in which the stressful stimuli (e.g. loneliness) will become a risk factor when the pre-existing cognitive processing approaches cannot compensate for the damage (Stern, 2012). This hypothesis cannot be tested in the current study.

In addition, the finding from the current study suggests that loneliness is not associated with dementia onset for the oldest old, which contradicts the findings by Holwerda et al. (2012) and Wilson et al. (2007) who reported a significant relationship between loneliness and onset of dementia.

Although testing the association between socio-demographic factors and cognitive decline was not the primary aim of the current analysis, the findings on the

association between age (here indicating cohort effect), sex and education are in line with findings from other studies (Amieva et al., 2005; Brayne et al., 1999; Dufouil et al., 2000; Jacqmin-Gadda et al., 1997; Matthews et al., 2012). In the current study, the impact of time on cognitive decline was not significant, this might be explained by the fact that participants with cognitive impairments may die earlier than those with better cognition at baseline, which indicates that average population cognitive decline is not as great as average individual decline (Matthews et al., 2012).

6.6 Conclusion

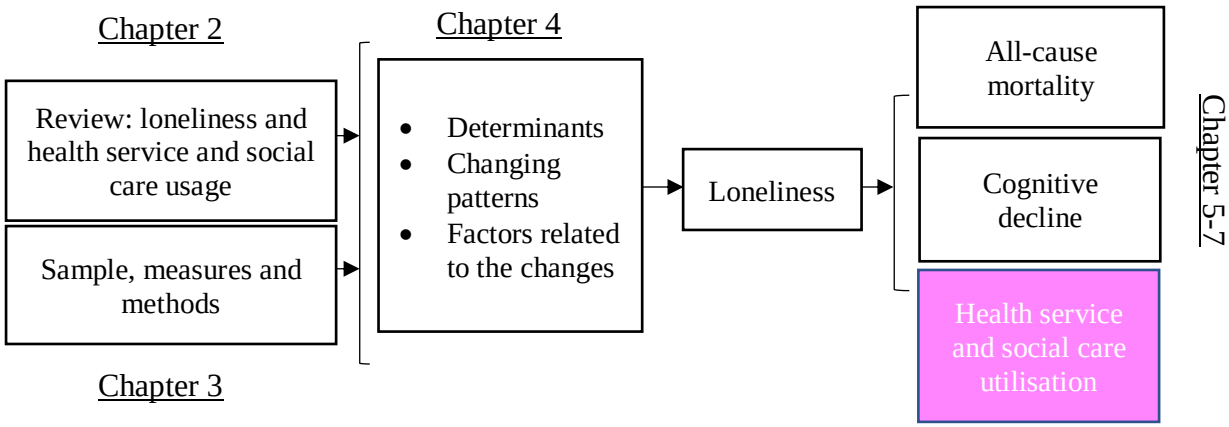
Loneliness is not a significant risk factor for cognitive decline for individuals at very old age. Accepting evidence from the younger old and assuming these generalise to the older old is challenged by these findings. There is a need to recognise greater complexity and differences in effects across age groups of different risk factors, as shown here for loneliness. Future studies with sub-analyses according to age would be helpful in confirming this. It is worth noting that the non-significant association between loneliness and cognition in the oldest old does not mean loneliness is not important; rather, it suggests that loneliness may not be a proximal risk factor for cognitive decline in this age group.

In Chapter 5 and Chapter 6, the effects of loneliness on mortality risk and cognitive decline over time were explored. In the next chapter, the association between loneliness and health service utilisation will be examined.

Chapter 7 Loneliness and health service and social care utilisation

7.1 Chapter Overview

This chapter explores the association between loneliness and health service and social care use in the oldest old.



7.2 Introduction

Chapter 2 synthesized the evidence for the associations between loneliness and health service and social care usage among individuals across all age groups. Evidence revealed two research gaps: (1) lack of evidence on the association between loneliness and community-based health service use and (2) lack of evidence on the association between loneliness and health service use among individuals who are at very late life stage. Despite the overall finding from Chapter 2 indicating that loneliness was not significantly and independently associated with health service utilisation, it is unclear whether loneliness is associated with increased demand for community services in the oldest old. As population is ageing across the world, there will be more older people approaching a very extreme age and being challenged by physical, mental and social changes. This might put them at higher risk of feeling lonely. On the other hand, older people prefer "ageing in place" (defined as "remaining living in the community rather than in residential care") (Wiles et al., 2012); this raises a need to develop various community services to support "ageing in place". Moreover, helping older people living in their homes and communities is assumed to be less costly than living in institutional care, therefore, "ageing in place" is not only preferred by older people themselves, but also is favoured by policy makers and health providers (World Health Organization, 2015). Taken together, it is very important to examine such assumptions and also the potential impact of loneliness on community-based health service usage in the oldest old.

The specific objectives of this chapter are:

(1) To examine the association between baseline loneliness (measured at wave 3) and health service and social care use (measured repeatedly at each wave) over a 7-year follow-up.
(2) To investigate the association between time-varying loneliness and health service and social care use (measured repeatedly at each wave) over the same follow-up period.

7.3 Methods

7.3.1 Participants

As with previous chapters (Chapter 4 and Chapter 5), data for current analysis were based on wave 3 to wave 5 of the CC75C study. Detailed description of CC75C is provided in Chapter 3.

7.3.2 Measures

Loneliness was the primary risk factor and was assessed by single-item scale. It had three levels: not lonely, slightly lonely and lonely (Chapter 3). Other individual-level factors used for current analysis were the same as those used in previous chapters, which included age (80-84, 85-89, and 90+), sex, physical impairments, number of doctor-diagnosed chronic diseases, depression, physical functioning limitations and cognition. Physical impairments were measured through a series of conditions including poor vision, poor hearing, arthritis/rheumatism, back pain, chest pain, shortness of breath, marked weakness in arms or legs, unsteady on feet, tendency to fall, trouble with nerves, and other, and were categorised into low, moderate and severe levels based on 25%, 50% and 75% percentiles. All measures were assessed at wave 3. Loneliness was also assessed at two additional waves: wave 4 and wave 5.

Health and social care utilization was the outcome and consisted of community service contact, hospital visit and general practice (GP) visit. Community service contact included the number of self-reported contacts with a home help, community nurse, meals on wheels and day centre in the past week. As most participants reported 6 or fewer contacts with each community service, answers to each community service use were topped at 6, with 6 indicating 6 or more. The hospital visit was assessed by asking participants how many times they have been in hospital in the past year; due to the small frequency of 2 or more visits, this variable was then topped at 2, with a value of 2 reflecting 2 or more. GP visit was measured by asking participants how long it is since they last saw a GP; original answers were recorded in months ranging from 0 to 98, a higher number reflected a longer time. However, as maximum numbers of other services use were recorded at 6, including a wide range of number

such as 0 to 98 would decrease the overall model fit. To improve the model fit, answers were re-coded in years and ranged from 0 to 9. Nevertheless, sensitivity analyses were conducted with the original coding of time since last visited GP (i.e. coded from 0-98) (Appendix 7.1, 7.2). In analyses, answers to community service contact and hospital visit were treated as count variables, and answers to time since last saw a GP were treated as a continuous variable.

7.3.3 Statistical analysis

To be eligible for current study, participants must have provided data on loneliness at wave 3. Loneliness non-response at wave 3 was adjusted by inverse probability weighting as explained in previous chapters. The characteristics of the sample were described according to the wave 3 loneliness level after adjusting for non-response. To examine the association between loneliness and health care utilization over a 7-year follow-up, the Generalized Estimating Equations (GEE) with independent working correlation structure and negative binomial family was fitted to modelling count outcome, and GEE with independent working correlation structure with Gaussian family was used to model continuous outcome. The use of GEE with independent working correlation structure is expected to ensure the target for inference is based on mortal cohort (Chapter 3). And the use of negative binomial modelling for count responses can help with overdispersion control in the data (Karazsia and Dulmen, 2008) (Chapter 3). Two types of associations were tested. First, the association between baseline loneliness (measured at wave 3) and health service use (repeated measurements at wave 3, 4, 5) was explored, and then the association between loneliness as a time-varying predictor (measured at wave 3, 4, 5) and health care utilisation was investigated. In both analyses, time was entered as t=1,2,3 to reflect the order of the three repeated measurements.

7.3.4 Missing data

As described in earlier chapters to adjust for dropout during follow-up, inverse probability weighting was used. The calculation was based on probability of staying in the study on the condition of responding to the previous wave and alive at the current wave (please see Chapter 3 for details). As participants in this study were

followed up from wave 3 onwards, to adjust for dropout before the start of wave 3, the cross-sectional weight was also applied. Taken together, a final weight was calculated by multiplying wave 3 cross-sectional weight, weight adjusting for loneliness non-response at wave 3 and longitudinal weight, and was implemented in analyses. All analyses were conducted in Stata v13.1 (StataCorp LP, College Station, TX, USA). A p-value <0.05 was considered statistically significant.

7.4 Results

7.4.1 Participants characteristics

The distribution of participants' characteristics according to loneliness measured at wave 3 is described in Table 7.1. As described in detail in Chapter 4 those who reported feeling lonely were more likely to be women, having a moderate to high level of physical impairment, depressed and having disabilities in IADL and ADL compared to non-lonely individuals. The characteristics of individuals who reported being slightly lonely were similar to those who reported feeling lonely.

Table 7. 1 The distribution of baseline characteristics by loneliness level (weight applied)

	Not lonely	**Slightly lonely**	**Lonely**	**p-value**
Age (%)				0.26
80-84	40	40	30	
85-89	40	50	40	
90+	20	10	30	
Sex (%)				<.001
Men	40	20	20	
Women	60	80	80	
Physical impairment (%)				<.001
Low	45	30	20	
Moderate	45	40	50	
High	10	30	30	
Number of chronic diseases (%)				0.13
0-2	70	70	60	
≥ 3	30	30	40	
Depression (%)				<.001
No	90	80	70	
Yes	10	20	30	
Physical functioning (%)				<.05
No disability	30	40	30	
IADL disability only	30	20	20	
IADL and ADL disabilities	40	40	50	
Cognition (mean(*sd*))	22.4 (6.2)	22.1 (6.3)	21.2 (7.01)	0.70

7.4.2 The association between loneliness and health and social care service utilisation

7.4.2.1 The association between baseline loneliness and health and social care service use over a 7-year follow-up

The association between baseline loneliness and health service utilization is shown in Table 7.2. Only feeling slightly lonely was significantly and positively associated with GP visits after adjusting for demographic characteristics and physical and mental health. Neither feeling lonely nor feeling slightly lonely was found to be related to home help use, community nurse contacts, meals on wheels service use, day centre and hospital visits. Results also indicated that moderate and high level of physical impairments were significantly associated with home help use and hospital visits. Having 3 or more chronic diseases was associated with community nurse contacts. Having disabilities in both IADL and ADL was related to increased frequency of day centre visits. On the other hand, depression was significantly and negatively associated with day centre visits. Being female and having at least 3 chronic diseases was associated with GP visits.

7.4.2.2 The association between time-varying loneliness and health and social care service use over a 7-year follow-up

When taking time-varying loneliness into account, individuals who reported being lonely had three times as many contacts with community nurses and meals on wheels services as those who were not lonely (Table 7.3). The other variables that were significantly associated with health care utilization were similar to those in the analysis exploring the association between baseline loneliness and health care use, except that the significance of the associations between depression, disabilities in IADL and ADL and day centre visits disappeared; instead, the high level of physical impairment was found to be significantly related to day centre visits.

Table 7. 2 The association between baseline loneliness and health service and social care utilization

	Home Help	**Community Nurse**	**Meals on Wheels**	**Day centre**	**Hospital visit**	**Time since last saw a GP**
	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	RR (95% CI)
Time	1.1 (0.4, 2.8)	2.5 (0.9, 6.9)	1.1 (0.4, 2.8)	0.9 (0.3, 2.6)	1.5 (0.7, 3.0)	1.0 (0.8, 1.3)
Loneliness (wave 3)						
Slightly lonely	1.3 (0.5, 3.6)	0.6 (0.2, 2.2)	1.9 (0.8, 4.9)	1.6 (0.5, 5.0)	1.3 (0.8, 2.1)	**0.8 (0.7, 0.9)**
Lonely	2.4 (0.8, 7.3)	1.1 (0.5, 2.5)	2.0 (0.9, 4.5)	1.4 (0.3, 5.3)	1.2 (0.8, 1.9)	0.9 (0.8, 1,1)
Age						
85-89	0.5 (0.2, 1.1)	0.8 (0.4, 1.9)	0.8 (0.4, 1.7)	1.0 (0.4, 2.3)	0.7 (0.5, 1.1)	1.1 (0.9, 1.3)
90+	0.9 (0.2, 3.9)	0.9 (0.3, 2.6)	0.6 (0.1, 3.6)	1.6 (0.1, 19.9)	1.3 (0.6, 2.9)	1.1 (0.7,1.7)
Sex						
Women	1.3 (0.5, 3.2)	0.7 (0.3, 2.0)	0.8 (0.4, 2.0)	1.4 (0.6, 3.4)	0.7 (0.4, 1.1)	**0.8 (0.6, 1.0)**
Physical impairments						
Moderate	**2.3 (0.96, 5.4)**	2.2 (0.9, 5.1)	0.6 (0.2, 1.5)	1.6 (0.4, 5.8)	1.3 (0.8, 2.1)	1.0 (0.8, 1.2)
High	**3.9 (1.5, 10.6)**	2.0 (0.8, 5.1)	1.9 (0.8, 4.6)	3.2 (0.7, 13.6)	**2.5 (1.4, 4.6)**	0.9 (0.7, 1.1)
Health condition						
≥ 3	1.5 (0.7, 3.3)	**2.4 (1.1, 5.0)**	1.2 (0.6, 2.5)	2.1 (0.7, 6.5)	1.1 (0.7, 1.7)	**0.8 (0.7, 0.96)**
Depression						
Yes	0.6 (0.2, 1.6)	0.6 (0.2, 1.9)	0.5 (0.2, 1.5)	**0.3 (0.1, 1.0)**	1.1 (0.5, 2.2)	0.9 (0.8, 1.1)
Physical functioning						
IADL disability only	2.4 (0.9, 6.4)	1.0 (0.3, 3.2)	0.8 (0.3, 2.6)	2.4 (0.9, 6.3)	0.7 (0.4, 1.2)	0.9 (0.7, 1.1)
IADL and ADL disabilities	2.3 (0.9, 6.2)	1.6 (0.6, 3.9)	1.5 (0.6, 3.7)	**2.9 (0.96, 8.9)**	1.0 (0.6, 1.7)	1.0 (0.8, 1.2)
Cognition	0.9 (0.8, 1.1)	1.0 (0.9, 1.1)	0.9 (0.8, 1.1)	1.0 (0.8, 1.1)	1.0 (0.9, 1.1)	1.0 (0.9, 1.1)

Reference groups: not lonely, 80-84 years old, men, no physical impairments, 0-2 chronic diseases, not depressed, and not disabled.

IRR: incidence rate ratio. RR: risk ratio.

Table 7. 3 The association between time-varying loneliness and health service and social care utilization

	Home Help	**Community Nurse**	**Meals on Wheels**	**Day centre**	**Hospital visit**	**Time since last saw a GP**
	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	RR (95% CI)
Time	1.0 (0.4, 2.5)	2.3 (0.9, 5.8)	1.0 (0.4, 2.6)	1.4 (0.4, 4.9)	1.3 (0.7, 2.6)	1.0 (0.8, 1.2)
Loneliness						
Slightly lonely	1.2 (0.5, 2.9)	0.8 (0.3, 2.6)	1.6 (0.6, 3.8)	1.7 (0.5, 5.5)	1.4 (0.9, 2.1)	0.9 (0.7, 1.03)
Lonely	2.0 (0.8, 4.9)	**3.4 (1.4, 8.7)**	**2.5 (1.1, 5.6)**	1.4 (0.4, 5.3)	1.5 (0.9, 2.4)	0.9 (0.8, 1.1)
Age						
85-89	0.5 (0.2, 1.1)	0.8 (0.3, 1.9)	1.0 (0.5, 2.0)	1.0 (0.4, 2.5)	0.7 (0.5, 1.2)	1.1 (0.9, 1.3)
90+	0.9 (0.2, 4.4)	1.3 (0.4, 4.7)	0.6 (0.1, 5.9)	4.2 (0.3, 51.7)	1.0 (0.4, 2.7)	1.2 (0.8, 2.0)
Sex						
Women	1.2 (0.5, 3.1)	0.5 (0.2, 1.5)	0.8 (0.3, 1.9)	1.4 (0.5, 4.0)	**0.6 (0.4, 1.002)**	**0.8 (0.7, 1.003)**
Physical impairments						
Moderate	2.3 (0.9, 5.7)	1.9 (0.8, 4.5)	0.7 (0.2, 2.0)	4.0 (0.7, 23.4)	1.3 (0.8, 2.1)	1.0 (0.8, 1.2)
High	**4.1 (1.6, 10.8)**	1.4 (0.4, 4.5)	1.9 (0.7, 5.3)	**7.6 (1.2, 48.7)**	**2.3 (1.2, 4.4)**	0.9 (0.8, 1.1)
Health condition						
≥3	1.5 (0.7, 3.3)	**2.6 (1.2, 5.5)**	1.2 (0.6, 2.6)	2.3 (0.6, 8.7)	1.2 (0.8, 1.9)	**0.8 (0.7, 1.0)**
Depression						
Yes	0.6 (0.2, 1.6)	0.5 (0.2, 1.5)	0.5 (0.2, 1.7)	0.3 (0.1, 1.1)	1.1 (0.5, 2.1)	0.9 (0.8, 1.1)
Physical functioning						
IADL disability only	2.1 (0.8, 5.6)	0.9 (0.3, 2.7)	0.8 (0.2, 2.6)	2.7 (0.9, 8.5)	0.7 (0.4, 1.3)	0.8 (0.7, 1.02)
IADL and ADL disabilities	2.3 (0.8, 6.3)	1.0 (0.4, 2.5)	1.5 (0.5, 4.5)	2.1 (0.7, 6.7)	1.0 (0.6, 1.7)	1.0 (0.9, 1.2)
Cognition	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)	0.9 (0.8, 1.1)	1.1 (0.9, 1.2)	1.0 (0.9, 1.1)	1.0 (0.9, 1.02)

Reference groups: not lonely, 80-84 years old, men, no physical impairments, 0-2 chronic diseases, not depressed, and not disabled.

IRR: incidence rate ratio. RR: risk ratio.

7.5 Discussion

7.5.1 Main findings

Results from this study indicate that loneliness is a significant risk factor for certain types of health services in the oldest old regardless of health conditions. In particular, feeling slightly lonely at baseline was associated with a shorter time since last GP visit (RR=0.8, 95% CI: 0.6, 1.0). When modelling the association between time-varying loneliness and health care usage, feeling lonely was found to be significantly associated with increased contacts with the community nurse (IRR=3.4, 95% CI: 1.4, 8.7) and use of a meals on wheels service (IRR=2.5, 95% CI: 1.1, 5.6). Results from the sensitivity analyses were similar with the results from the main analyses (Appendix 7.1, 7.2).

7.5.2 Strengths and limitations

This study has several strengths. The use of data from one of the longest-run prospective cohort studies of the very old makes the repeated measures of loneliness and outcome variables at different time points possible; by using the repeated measurements, the association between loneliness and health service utilization can be examined more thoroughly. Moreover, as CC75C collected data on different types of health services, the impact of loneliness on health service use is investigated in a broader way than previous studies did; in particular, the association between loneliness and community service use is addressed in the current study. Furthermore, the use of weights can minimise the effect of non-response to the findings and reduce bias due to dropout (Jones et al., 2015).

However, the findings should be interpreted with caution. The use of self-reported health service utilization may introduce recall bias. It is unlikely to have effects on the findings as for most interviewed participants, their proxy informants were also interviewed, and answers from both were compared and the most reliable answers used (i.e. if answers were different, then proxy informants' answers were selected for participants who had mental problems) to minimize the differences. Another consideration is that, as in previous studies (Gerst-Emerson and Jayawardhana, 2015), disability was included as one of the covariates, and it was determined by whether participants needed help from family, friends or neighbours for performing at least one of their daily activities, such as cooking or doing housework. This type of help can be regarded as informal health care; therefore, it is possible that participants who can obtain informal care may use fewer community services. Although this might dilute

the association between loneliness and health care utilization, it was unlikely to change the direction of the association.

7.5.3 Interpretation of findings

The finding of loneliness and its association with GP visit is consistent with the finding from a previous UK population-based study, though there are slight differences between the two studies. In our study, compared to non-lonely individuals, we found that those who felt slightly lonely had a shorter time interval since they last visited their GP; whereas, in their study, they found that individuals who felt lonely tended to visit GPs about twice as often as individuals who were non-lonely (Ellaway et al., 1999). The explanations for the link between loneliness and frequent GP visits might be that GPs are easily accessible, and more importantly, a long-term relationship between patients and GPs can be easily developed. GPs are familiar with their patients' health conditions and emotional changes; as a result, a trust might be built within this relationship. Indeed, Ellaway and colleagues explained that older people who felt lonely and did not have family members or friends around them tended to regard their GPs as their confidants (Ellaway et al., 1999). Similarly, data from 'Campaign to End Loneliness' suggest that more than 75% of GPs and one in ten doctors reported seeing about 1 to 5 or 6 lonely people in a day (Cooper, 2013). These findings suggest that numerous lonely individuals are aware of their loneliness and make this known to medical professional. Findings also highlight the importance of emotional supports (e.g. having confidantes). However, unlike feeling slightly lonely, feeling lonely was not found to be significantly associated with a shorter time interval since they last visited their GP. This may be explained by the fact that lonely individuals were more likely to have health problems than slightly lonely individuals (Table 4.1 in Chapter 4); the association of feeling lonely with GP visits was explained by the association between health conditions and GP visits.

This study firstly examined the association between loneliness and community nurse contacts and use of a meals on wheels service in the oldest old. The independent significance of associations controlling for physical and mental health implied that similar to GPs, community nurses or meals on wheels service providers may have a hidden role in providing social interactions. For example, in a fixed randomized control study investigating the role of a home-delivered meals programme on 626 American community-dwelling seniors' feelings of loneliness, researchers reported that compared to control groups (i.e. individuals who received meal delivery once a week and individuals who remained on meal delivery waiting list), those who received their meal delivery on daily basis experienced decreases in their

loneliness, and the reduction was explained by the meal-delivery services indirectly providing more opportunities to elders for social interactions (Thomas et al., 2015).

On the other hand, neither feeling slightly lonely nor lonely was significantly associated with home help service use, day centre visit or hospital visit. Evidence from systematic review in Chapter 2 showed that lonely women expressed higher demands for domestic help than non-lonely women. The heterogeneity in findings might be related to the differences in statistical methods used. For example, apart from conducting comparison analysis, previous studies did not further test the association between loneliness and domestic help usage by performing advanced statistical analysis (Berg et al., 1981). While, in current analysis, the participants' socio-demographic and co-morbidities were taken into account. The non-significant association between loneliness and hospital visit is generally in line with other studies (Bock et al., 2017; Gerst-Emerson and Jayawardhana, 2015; Molloy et al., 2010; Newall et al., 2015), which reported that loneliness was not linked to hospitalisation or planned hospitalisation after controlling for initial health. These results indirectly support the assumption that lonely individuals visit their GPs or contact their community nurses more often not for medical advice but rather to seek opportunities to satisfy their needs for social interaction and stimulation.

Although cognitive function was not the primary risk factor, the lack of a relationship of cognition with service use merits discussion. One possible reason was that individuals who were cognitively impaired received informal care more often than those without impairment. Individuals who were cognitively impaired are more likely to be in a care setting, and are less likely to receive community health services. Additionally, the absence of significant correlations between depression, disabilities and day centre visits in time-varying model might be explained by the association between physical impairments (suffering from poor sight, back pain, chest pain, etc.) and day centre visits. Longitudinal analyses have reported that depression had significant impact on physical health; it increased the risk of sight problems, asthma, hypertension and cardiovascular disease (Kang et al., 2017). Furthermore, results from multi-state modelling in Chapter 4 suggested that depression and disabilities (limited physical functioning) were associated with increased loneliness. The emergence of significant relationships between time-varying loneliness and community nurse contacts and meals on wheels services use may also explain the disappearance of association between depression, disabilities and day centre visits.

7.6 Conclusion

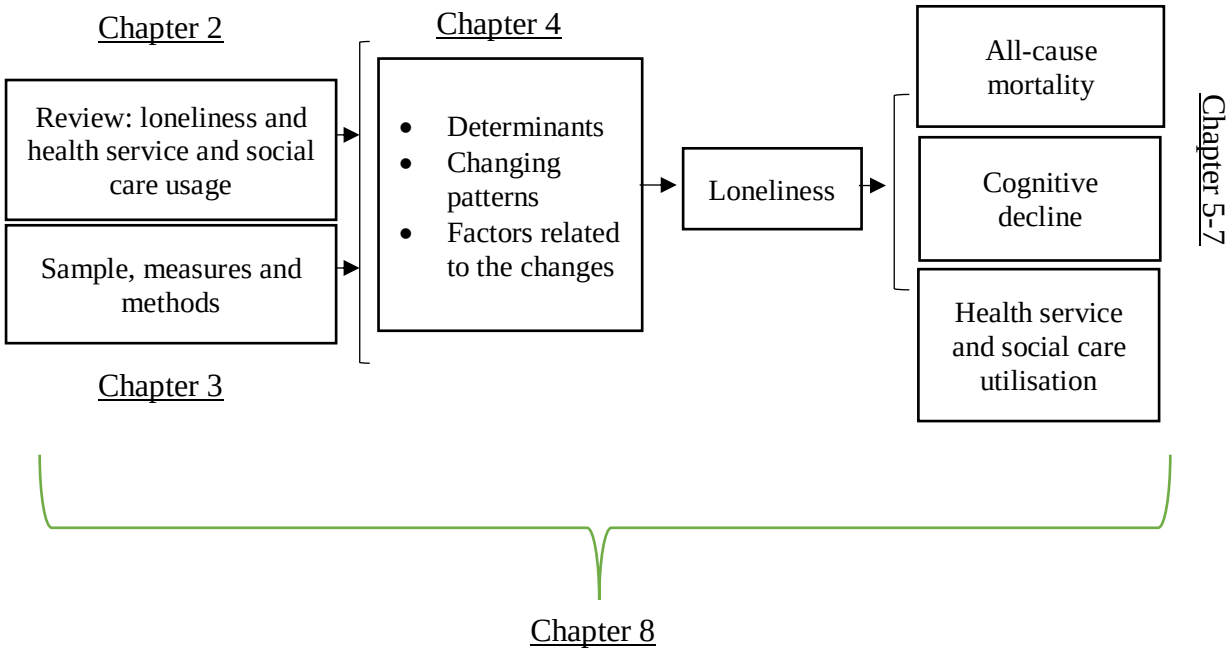
This chapter shows that loneliness was associated with more frequent GP visits, community nurse contacts and meals on wheels service usage, independently of participants' health conditions. Increasing public awareness of loneliness and developing effective interventions should be on public officials' agenda.

Chapter 8 Discussion

8.1 Chapter Overview

The aim of this chapter is to summarise, synthesise and discuss the findings from the previous seven chapters. This will be accomplished through:

(1) Providing an overview of the main findings from each previous chapter
(2) Discussing the strengths and limitations of the thesis
(3) Discussing the implications for public health
(4) Discussing areas for future research



8.2 Introduction

Previous research into social relationships and health indicates that deficits in social relationships - in both a quantitative and qualitative way - can have significant impact on individuals' health and well-being. The work presented in this thesis focused on loneliness - a subjective, distressful feeling that results from the discrepancy between desired and obtained social relationships and is characterised by a deficit in social relationships. Despite numerous studies that have been completed in this field, loneliness as a significant social relationship problem has not been the focus of studies of the oldest old. Given the ageing of the global population, with rapidly expanding numbers of the very oldest old along with changing societal structures, maximising the knowledge to be gained from studying existing population cohorts is important to guide future research and policy. Therefore, the overarching aim of this thesis was to provide evidence on the significance of loneliness in the oldest old. Its specific objectives included: what factors affected the feelings of loneliness, how it related to health (i.e. all-cause mortality and cognition), and whether it was associated with increased demands for health services and social care.

Figure 8.1 provides the summary of the research process. First, background literature was reviewed; it summarised the previous work on conceptualisation of social relationships, its relevance to health, as well as the mechanisms underlying the association between social relationships and health. Then the conceptualisation of loneliness, its determinants and health consequences and pathways linking loneliness to health outcomes were synthesized (Chapter 1). The results from the literature review emphasized the role of social relationships in health and supported an association between loneliness and health problems in older people.

A few studies have investigated the effect of loneliness on health service and social care utilisation, but the overall evidence on such association was limited; therefore, a systematic review on this topic was conducted (Chapter 2). In addition, since previous evidence on the determinants of loneliness, and on the relationship between loneliness and health, as well as on health service and social care usage, were almost exclusively based on an older population with the oldest old under-represented, data from the

CC75C study (Chapter 3) allowed for the exploration of risk factors of loneliness (Chapter 4), and the impact of loneliness on health and health services use in the oldest old (Chapter 5-7). The following chapter will discuss the key findings, the strengths and limitations, the public health implications, and the future research direction.

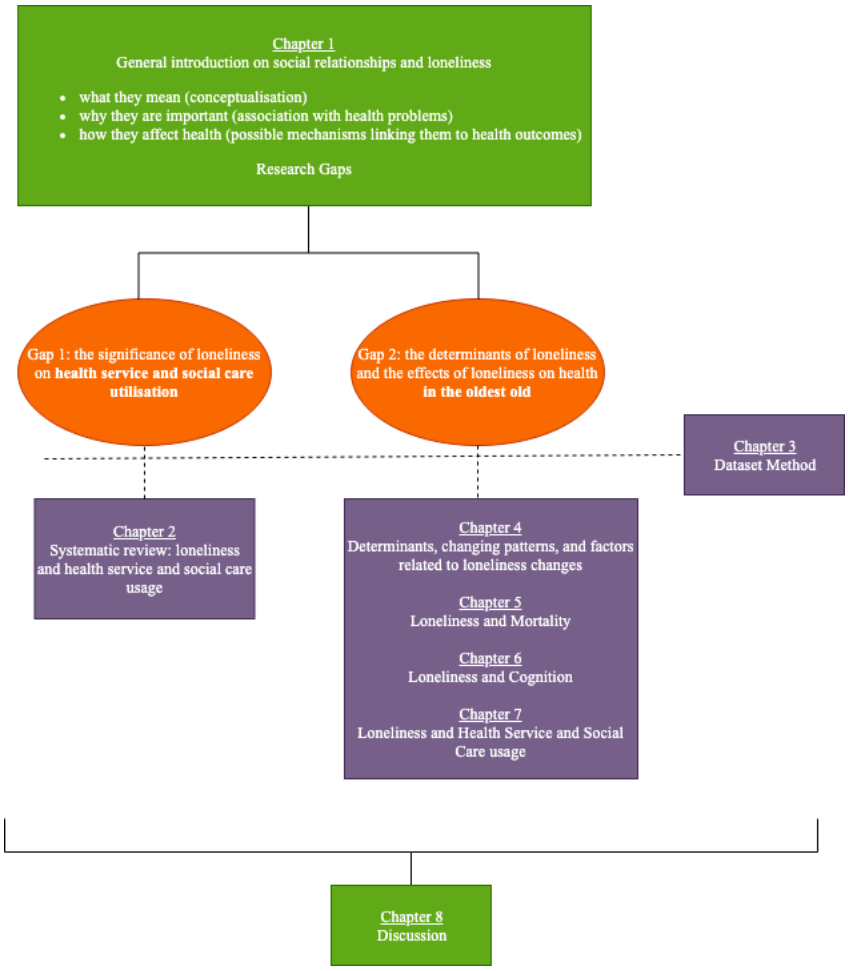


Figure 8. 1 Overview of research process

8.3 Key findings

8.3.1 Reviews and Syntheses

Loneliness, as a burgeoning area of interest, has been studied for years. Chapter 1 provided a clear view of historical approaches to loneliness through a comprehensive literature review. Moreover, since loneliness and social isolation were used loosely in

literature, Chapter 1 placed an emphasis on distinguishing between these two related but distinct concepts. Further, to capture the significance of loneliness, the determinants and health consequences of loneliness were explored. In order to understand the role of loneliness in health, possible mechanisms underpinning the association between loneliness and health outcomes were investigated.

In order to learn whether loneliness was associated with increased demands for health and social care services, a systematic review of the association between loneliness and health service and social care usage was conducted. This review expanded the previous review (Valtorta et al., 2018) by including participants in all age groups and residing in different countries, highlighting the heterogeneity in the conceptualisation of loneliness and in the included health and social services, emphasising the need for incorporating a wider range of social care services in future research.

8.3.2 Loneliness: determinants, changing patterns and factors associated with loneliness transitions

Having examined loneliness from theoretical and conceptual perspectives, the next step was to move forward to empirical analyses. The first analysis was to investigate the risk factors of loneliness, the changing patterns of loneliness over time and the factors related to loneliness transitions. The results of this analysis placed an emphasis on widowhood, especially recent widowhood, and the qualitative aspects of social contacts on loneliness. These were consistent with previous findings based on different conceptualisation models. For example, the quality of social relationships was found to be one of proximal factors of loneliness in filtration model and a key determinant in social relationship model (Chapter 4).

However, although the analysis presented here included a wide range of risk factors, potential risk factors that were identified in previous models are not available in the CC75C dataset (e.g. opportunities of social contacts, financial condition, self-efficacy in MODEL model; Chapter 4). Self-efficacy was shown to be the most important risk factor of loneliness in MODEL related to the initiation and maintenance of social behaviours, such as building new relationships. Reduced self-efficacy in older people may be related to deterioration in physical function and loss of social connections that

can be associated with ageing, as well as the lack of social skills. Despite this limitation in these analyses, the risk factors for loneliness presented in these analyses are unique with respect to direct exploration of relationships between risk factors and loneliness.

As mentioned in Chapter 4, risk factors of loneliness in the oldest old were also explored in a previous study (Brittain et al., 2017). To further illustrate the picture of loneliness in the oldest old, the comparisons of empirical findings between Brittain's study and the current study were listed in this section. In general, results from cross-sectional multivariable analyses of risk factors of loneliness were consistent (Table 8.1), though there were differences in study samples (in Brittain et al. study, all participants were aged 85 years at baseline) and variations in loneliness (they categorised participants into 'never lonely', 'sometimes lonely' and 'always/often lonely' groups) as well as other variable measurements.

Table 8. 1 Comparisons of results of multivariable analyses of risk factors of loneliness between the Brittain et al. study and the current study

Investigated risk factors	Brittain et al. 2017	Current analysis
Age	√	√
Sex (being women)	√ *	√
Widowhood	√ *	√ *
Living arrangements (living alone)	√ *	√ *
Education	√	√
Quantitative aspect of social contacts	-	√
Qualitative aspect of social contacts	-	√ *
Perceived physical health	√	√
Sight, hearing problems	-	√ *
Disability	√	√
Depression	√ *	√ *

Note: * indicates a significant association ($p<0.05$) was found for that specific factor and loneliness. '√' indicates the specific risk factor was included in the analysis; '-' indicates the specific risk factor was not included in the analysis

In the current analysis, over 60% of individuals experienced loneliness at some time during a 7-year follow-up, of which about a quarter had increased loneliness. Similar changing trends of loneliness were reported in Brittain et al. study, though participants in their study were followed up for only 3 years (Brittain et al., 2017) (Figure 8.2).

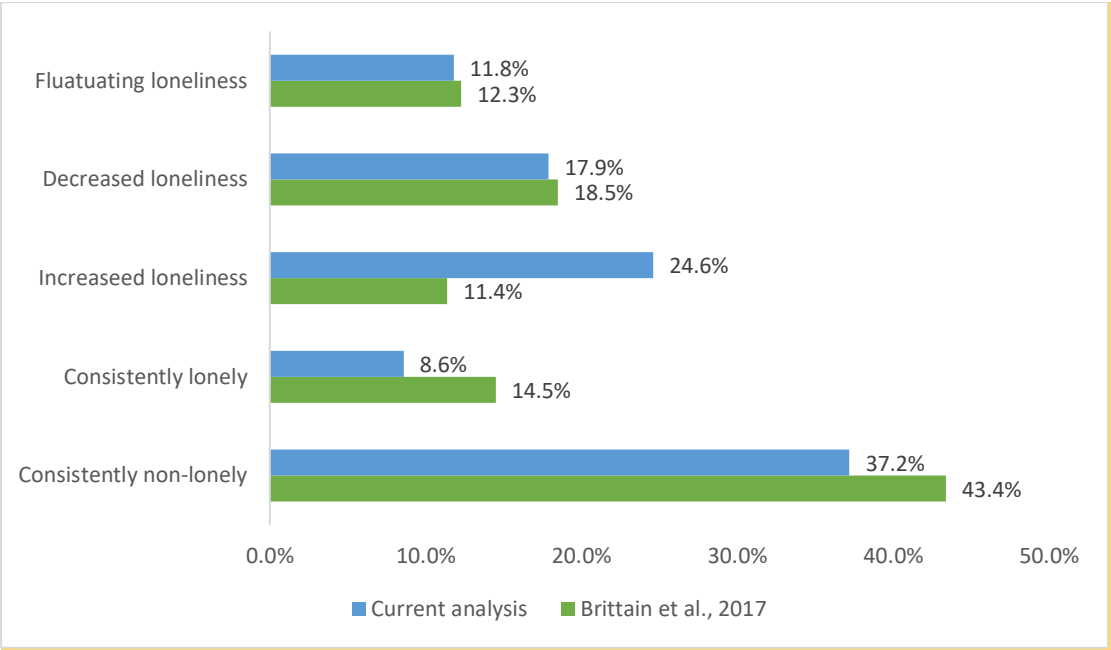


Figure 8. 2 Comparisons of changing patterns of loneliness over time between the Brittain et al. study and the current study

The current study further analysed the predictors of loneliness transitions; results revealed that having a lower level of physical functioning and more severe depression were associated with loneliness transitions from slightly lonely status to lonely status (Chapter 4). Overall, findings from the current study were important in several ways. Firstly, they supported the notion that deficits in the qualitative aspect of social relationships, rather than less frequent social contacts, enhance the likelihood of experiencing loneliness; this reflected the conceptualisation that loneliness is a subjective evaluation of the discrepancy between obtained and desired social relationships (Chapter 1). Secondly, the association between depression and increased loneliness suggested that the psychological factor was linked to the increased likelihood of loneliness deterioration (i.e. becoming lonelier).

This thesis provides, as far as the searched literature reveals, the first analysis of risk factors for loneliness transitions in the oldest old. Previous studies focusing on identification of risk factors for loneliness transitions were based on data from two waves that can only capture the transition from non-lonely status to lonely status or vice versa. By using data from three waves, the risk factors associated with transitions between different levels of loneliness, e.g. from non-lonely status to slightly lonely

status, or from slightly lonely status to lonely status, were able to be identified. Moreover, the use of multi-state modelling in this analysis enabled us to model the transitions from each loneliness status to death, which has not been explored in previous studies. Therefore, this analysis provided new evidence of the association between risk factors and loneliness transition in the oldest old.

8.3.3 The impact of loneliness on health: all-cause mortality and cognition

The impact of loneliness on all-cause mortality and cognitive decline has been explored in numerous previous studies; but most studies measured loneliness at a single time-point rather than assessing it repeatedly. Health implications over time cannot be captured by such designs. Here, the impact of loneliness (loneliness was treated as a time-varying risk factor) on mortality and cognition was investigated by using data spanning across more than two waves. The results of these analyses indicated that repeated exposure to loneliness was not associated with increased risk of mortality and cognitive decline.

The non-significant relationship between loneliness and mortality in the current study was contradictory to previous findings that loneliness was an important risk factor for mortality (mentioned in Chapter 1). This apparent inconsistency may due to the fact that different studies investigated different mechanisms that could underpin loneliness and mortality. For example, Tilvis et al. (2011) did not include physical health and psychological factors (e.g. depression) in their analysis. In the current study, the number of chronic diseases, physical functioning and depression were all included. In Luo et al. (2012) study, a mediation analysis was conducted to test whether emotional health (effectively depressive symptoms), self-rated physical health and functional limitations mediated the association between loneliness and mortality and concluded that functional limitations and self-rated poor health, but not depressive symptoms, constituted proximal mechanisms through which loneliness affected mortality. This partly supports results presented here in which, after controlling for the number of chronic diseases and physical functioning, the effect of loneliness on mortality was attenuated. In a cross-lagged model, Luo and colleagues also reported a significant reciprocal relationship between loneliness and depressive symptoms (i.e. the 2-year

cross-lagged effect of loneliness on depressive symptoms was significant and the 2-year cross-lagged effect of depressive symptoms on loneliness was also significant), which supported previous findings that the link between loneliness and depression are in a potential vicious cycle. The reciprocal relationship between loneliness and depression was not tested in this thesis, rather, depression predicted loneliness transition and attenuated the effect size of mortality risk of loneliness.

In addition, as mentioned above, previous studies often measured loneliness once (at baseline), whilst loneliness was treated as a time-varying risk factor in the present study. Furthermore, unlike any previous studies, the current study exclusively focused on the oldest old, the fact that the 5-year mortality risk of loneliness remained after adjusting for health conditions (Appendix 5.3) suggested that ageing-related health changes may play a fundamental role in mortality at very old age.

8.3.4 Loneliness and health service and social care usage

As pointed out in Chapter 2, the evidence on loneliness and health and social care service usage was limited. To address this research gap, analysis exploring the effect of loneliness on health service and social care utilisation was conducted. In order to better understand the nature of any associations, the associations between loneliness and service usage were measured at one time-point (i.e. wave 3), as well as at multiple time-points. Findings were heterogeneous. Baseline loneliness was associated with a shorter time since last GP visit; the exposure to loneliness over time was associated with higher frequency of nurse visits and use of meals on wheels services. It is likely that individuals who felt constantly lonely were less likely to have a sense of security and more likely to experience other health-related problems that require external assistance.

8.4 Strengths and limitations

8.4.1 Strengths

A key strength of this thesis comes from its grounding in the multidisciplinary literature. Different theoretical frameworks of loneliness were discussed in Chapter 1. In addition, various approaches to assess loneliness were reviewed. Without being informed by the comprehensive review of loneliness in both historical perspective and current research-driven perspective, it would not have been possible to understand the scope of loneliness and capture the core component of loneliness.

Another major strength is that all empirical analyses in this thesis regarded loneliness as a time-varying factor. Unlike previous studies in this field, by using data from more than two waves in this thesis, another aspect of loneliness – its changeability over time – was captured. Moreover, with repeated measures of loneliness, associations between loneliness and health outcomes could be investigated more thoroughly.

Additionally, unlike depression or generalised anxiety disorders, loneliness is not a clinical disorder, therefore there is no symptom threshold at which loneliness is 'diagnosed'. When differentiating different levels of loneliness, for the ease of statistical model building, most previous studies either treated loneliness as a continuous variable with higher score reflecting a greater level of loneliness (Cacioppo et al., 2002; Coyle and Dugan, 2012; Luo et al., 2012) or dichotomized responses into non-lonely and lonely status; for example categorising the frequencies of always, often and sometimes lonely as lonely status, and categorising the frequencies of seldom and never lonely as non-lonely status (Holmen and Furukawa, 2002). Treating loneliness as a continuous variable limits ability to explore the differences between different types of loneliness, and dichotomizing responses may result in information loss, which further limits the ability to better capture the nuances of loneliness. Although throughout this thesis the responses of "lonely" and "very lonely" were combined as one category due to the small frequency of responses, three different intensities of loneliness were retained.

Only data from wave 3 and onwards were used in empirical analyses rather than data from baseline as explained in earlier chapters. This could introduce survival bias, and to address this possibility, a weight that adjusted for dropout from baseline wave to wave 3 was computed and implemented.

At baseline, the CC75C samples was highly representative of people aged 75 and over living in Cambridge given its response rate over 90%. All interviews were conducted by trained interviewers, and at each interview a similar questionnaire was administered. This ensured the consistency of data across waves. Data collected at each wave covered a wide range of factors, ranging from basic demographic characteristics, health conditions, activities of daily living to the detailed assessments of cognitive function. The diagnosis of cognitive function was based on the structured assessments, which ensured the diagnostic standards. In order to continuously keep the study sample representative and minimise the lost to follow-up due to frailty, the proxy informants were interviewed where the frail participants might otherwise have dropped out (Fleming et al., 2007).

The study exploring the cross-cultural perspectives of loneliness qualitatively captures the perspectives of laypeople. The study was not intended to produce generalizable findings, but to further deepen the understanding of loneliness by exploring the perspectives of individuals whose evaluations of loneliness have not been previously captured. It offers new insights into the nuances and diversity in conceptualisation of loneliness. Common features and differences in conceptualisation of loneliness were highlighted between individuals and across countries.

8.4.2 Limitations

In CC75C, loneliness was assessed by the single-item scale “Do you feel lonely?”. This approach presumes loneliness as a unidimensional concept and a common understanding of the concept between individuals, which is highly subject to cultural context (Jylha, 2004). Moreover, because of its simple nature, it assumes that the primary difference between individuals is in the intensity of the experience. More importantly, it may not be able to measure the true prevalence of loneliness.

Loneliness might be seen as a stigmatizing concept associated with shame, guilt and failure, therefore people may not want to define themselves in this way, and consequently give an inaccurate response. Nevertheless, the single-item scale is easy to implement in a large survey. It has been widely implemented in European-based studies and found to be well accepted by older participants (Victor et al., 2005a). The baseline wave of the CC75C study was highly representative of the 75+ population living in Cambridge. Subsequent waves lose some of this representativeness due to the attrition through mortality or dropout. Although cross-sectional weight for wave 3 (i.e. data from wave 3 was regarded as the baseline data in this thesis) was computed to minimise the bias due to attrition, it is likely that bias does still exist. Further, missing data at each wave remains problematic, despite several methods such as multiple imputation, inverse probability weighting or sensitivity analysis being used (Chapter 3) in subsequent analyses; caution should be taken when interpreting the findings.

Although physiological (e.g. dose-response relationship between loneliness and cardiovascular, cortisol awakening response, etc.) and non-physiological (e.g. health behaviours) pathways linking loneliness to health have been proposed (Caspi et al., 2006; Pressman et al., 2005; Dyal et al., 2015) and were discussed in Chapter 1, the analyses could not further investigate these factors as mediators using the CC75C dataset. The association between loneliness and all-cause mortality was explained by physical health (e.g. number of chronic conditions) and psychological factors (e.g. depression) (Chapter 5), and the association between loneliness and cognition was explained by age, sex and educational level (Chapter 6); these might indirectly support the mechanisms underpinning the association between loneliness and health outcomes.

Despite the CC75C including individuals living in institutions, subgroups analyses cannot be conducted due to the small number of institutionalised individuals. Previous research based on older nursing home residents (aged 65 and over) without cognitive impairments reported a high prevalence of loneliness (56%) (Drageset et al., 2011), which indicates that individuals living in care settings are less likely to maintain the emotional closeness with significant others or develop strong attachments; however, it

is also possible that living in care settings provides an opportunity for elders to build new social relationships that otherwise have not been developed if living in communities alone. The experience of loneliness may also differ across other subgroups, such as gender. Compared to women, men are more likely to rely on marriage to find an intimate attachment, whereas women can find such attachments from other social circles. Therefore, the marital differences in loneliness are greater among men than women (Dykstra and de Jong Gierveld, 2004). This study was not able to explore the associations between loneliness and health outcomes between various subgroups as it would need a larger sample size than CC75C to detect any differences.

CC75C was based on an earlier generation and that experiences may change over time as society and family structures change. For example, family size is getting smaller. According to the office for national statistics (ONS), the average completed family size for women aged 45 today (born in 1967) is 1.91; it is 2.36 for their mothers' generation (born 1940) at the same age (McConnell et al., 2007). Divorce rates have experienced a dramatic rise in late 1960s and early 1970s and a decrease in 1990s (Haines, 2017). Individuals' perception of family or social relationships could be influenced by these changes. However, findings from Chapter 4 are supported by studies based on recent cohorts (relatively young old), suggesting that despite of the changes in society and family structures, the qualitative aspect of social relationships rather than the quantitative aspect of social relationships is closely related to loneliness across time.

According to the social epidemiological conceptual framework developed by Berkman and Kawachi (2000, mentioned in Chapter 1), the place where an individual resides, the culture, politics and social value attached to that place, have a great potential to influence and shape individuals' social relationships. Therefore, by using data from a single dataset that only included samples living in Cambridge, the findings presented in this thesis may not be generalizable to a population in other settings. However, national datasets of the very old are rare as the cohorts are subject to significant dropout rate due to the morbidity and mortality given their advanced age. Nevertheless, a few studies exist, such as the Newcastle 85+ study. Future

studies based on other datasets like the Newcastle 85+ study are needed to produce comparisons with the findings from the CC75C study.

8.5 Public health implications

Loneliness, as a growing research topic, not only attracts attention from researchers, but also receives increasing attention from policy makers. In 2011, a national campaign "The Campaign to End Loneliness" was launched and governed by Age UK Oxfordshire, Independent Age, Manchester City Council, Royal Voluntary Service and Sense. The purpose of this campaign is to raise public awareness of loneliness among older people, and to ensure that public officials at national and local levels can recognise the importance of loneliness and make it a public health priority (The Campaign to End Loneliness, 2011). Recently, in January 2018, a first minister for loneliness was appointed by the Prime Minister Theresa May. In the statement, Theresa May said *"For far too many people, loneliness is the sad reality of modern life. I want to confront this challenge for our society and for all of us to take action to address the loneliness endured by the elderly, by carers, by those who have lost loved ones – people who have no one to talk to or share their thoughts and experience with"* ("Minister for loneliness appointed to continue Jo Cox's work", 2018).

Thus far, efforts to tackle loneliness have been mainly focusing on improving social skills, enhancing social support, increasing opportunities for social interaction and addressing deficient social cognition (Masi et al., 2011). This thesis provides new angles to tackle the loneliness issue in the oldest old through identifying risk factors for loneliness (primary prevention), screening at-risk groups (secondary prevention), and decreasing social stigma via acknowledging the multi-facets of loneliness (tertiary prevention) (Figure 8.3). Furthermore, to inform prevention strategies and policies at a wider societal level, a novel ecological model integrating social and cultural contexts is proposed.

8.5.1 Implication for primary prevention – developing individual-tailored programmes

Despite the various prevention and intervention programmes, few have been found to be effective (Cattan et al., 2005; Masi et al., 2011). One of the reasons for this might be that the available programmes did not differentiate the specific triggers for loneliness. For example, a befriending service is intended to help individuals to combat loneliness by providing social interaction opportunity through telephone calls. This might be effective for individuals who feel lonely due to lack of social interactions because of morbidity but for those whose loneliness results from other sources, such as bereavement or lack of perceived high-quality social relationships, a befriending service is unlikely to be effective. In the analysis of determinants of loneliness conducted in chapter 4, widowhood, living alone, feeling unsatisfied with social contacts, having sight or hearing problems and depression were found to be associated with loneliness. For the situation that is potentially modifiable, such as having perceived unsatisfying social contacts, physical health problems and depression, programmes that target improving social cognition, physical and mental health may decrease individuals' likelihood of experiencing loneliness; for situations that cannot be avoided, such as widowhood, offering professional counselling services may help to prevent loneliness. Identifying a wide range of potential risk factors, developing diverse prevention programmes and making them readily accessible could help prevent the experience of loneliness.

8.5.2 Implication for secondary prevention – regularly screening 'at risk' groups

Previous intervention programmes have incorporated various research designs and research settings. Most are group-based interventions (i.e. social support groups, social activities, videoconferencing) (Stewart et al., 2001; Tsai et al., 2010). A few were one-to-one interventions (i.e. home visiting, animal-assisted therapy) (Banks et al., 2008; Fokkema and Knipscheer, 2007). The programmes either target community-dwelling people or institutionalised individuals. Nevertheless, these programmes mainly focus on improving participants' social skills, providing social interaction opportunities, enhancing social support and improving social cognition. In spite of the variety and the diversity in the current intervention programmes, all are short-term.

Loneliness can change over time (Chapter 4); providing a challenge for interventions to account for the factors that influence the changes of loneliness. Because of the complexity, no successful initiatives have been developed (Dickens et al., 2011). Building a robust, long-term monitoring service might be an alternative effective way to identify 'at risk' groups and therefore to further reduce loneliness.

8.5.3 Implication for tertiary prevention – reduce social stigma via acknowledging the multi-facets of loneliness

Loneliness as an indicator of a social deficit has been reported to be linked to social stigma (Rook, 1984). In particular, lonely individuals are more likely to withdraw themselves from social life and be less accepted by others (Lau and Gruen, 1992). In addition, when measuring loneliness, to avoid public criticism lonely individuals often give answers which they think are publicly acceptable, such as down-labelling their loneliness level (Victor et al., 2005a). Furthermore, the findings from previous qualitative studies as well as from Chapter 8 indicate that loneliness is seen as a vulnerability, failure, and a social skill deficit. Most often, the public think lonely individuals should be blamed for their own loneliness. Improving public awareness of loneliness, especially placing an emphasis on the causes of loneliness, may help the public understand the complexity of loneliness, and therefore potentially reduce social stigma towards lonely individuals. In addition, when developing interventions, researchers and policy makers should acknowledge to participants that feeling loneliness is a personal feeling, it is not a psychological problem and should not be associated with shame or guilt. Moreover, social media can help with raising public awareness of loneliness, act as an educational channel and introduce the availability of professional services.

Connecting lonely individuals with the correct service is very important. In Chapter 7, slight loneliness was found to be associated with frequent GP visits. A good GP-patient relationship may provide services beyond medical needs, such as social and emotional support, which indirectly may help with reducing lonely feelings. However, from a GP's point of view they are constrained by lack of time. In addition, as reported by "Campaign to End Loneliness", about 1-5 patients per day visit their GP not because of medical conditions but because they are lonely. This produces more

pressure on GPs as this is a condition without a therapeutic solution; loneliness reflects individuals' personal experience, triggers for loneliness vary between individuals as well coping skills. Taken together, the limited options to support people affected by loneliness and lack of time make it difficult for GPs to help with lonely patients (van der Zwet et al., 2009). On the other hand, health services across world are experiencing financial constraints. In the UK, the funding gap keeps increasing in the National Health Service (NHS), estimated to reach to £30 billion by 2020 (NHS Five Year Forward View, 2016). Given the dramatically increasing financial burden, the need for developing an effective strategy to distribute the existing healthcare services and balancing health-related costs is highlighted. It is in this context, along with the need to connect people with appropriate services, that social prescribing has become popular. Specifically, social prescribing offers GPs an option to refer their patients to the existing non-medical community services to help improve health and well-being (Bickerdike et al., 2017). Although the current social prescribing pilot programmes are small-scale, and there is no robust evidence to support their effectiveness, the findings from Chapter 7 do suggest that social prescribing, as a tertiary strategy, could help decrease the burdens of loneliness on health service and social care delivery.

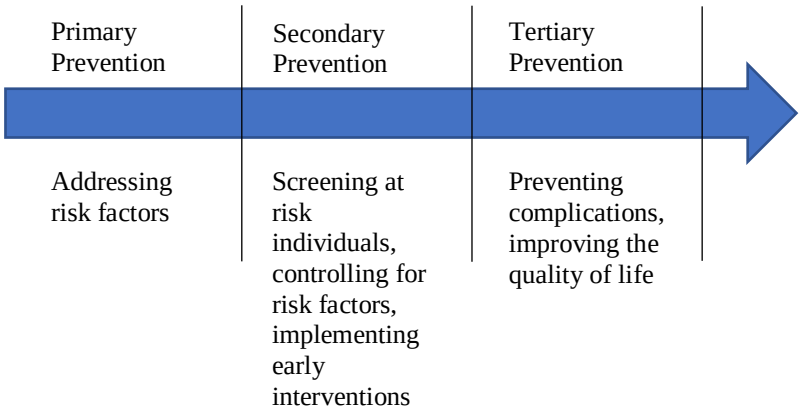


Figure 8. 3 Summary of different levels of interventions

8.5.4 A novel ecological approach to tackle loneliness – beyond the current research

Durkheim developed an ecological approach to explain the variations in suicide rate across nations (Chapter 1, section 1.1.2). One question would be whether this ecological approach could be applied to loneliness? How can potential primary prevention strategies be integrated within this approach?

From a social epidemiological conceptual framework (Chapter 1, section 1.1.2), we know that social and cultural contexts (macro level factors) can influence individuals' perception of social relationships, the way they engage in social activities and build social connections (mezzo level factors), which further influence individuals' psychological feelings and health behaviours (micro level factors). Previous evidence has found a North-South divide of European nations with regard to the prevalence of loneliness (Jylha and Jokela, 1990; Yang and Victor, 2011). That is, people living in northern European countries are generally less likely to report loneliness than those living in southern Europe, despite a general perception that the latter have greater intergenerational connection and sociability. The explanation given by researchers is this: northern European countries emphasize the values of individualism, whereas, in southern European countries, the culture typically values interdependence (Adams et al., 2004: 324-325). In this sense, if living alone is associated with loneliness, it is understandable that individuals in southern Europe who are living alone are more likely to report loneliness when their expectation is to be living together with family members (Jylha and Jokela, 1990). Furthermore, evidence also suggests that social change may play a role in the experience of loneliness. In addition to the North-South difference with regard to the prevalence of loneliness, Yang and Victor (2011) also found that Eastern Europe had a high prevalence of loneliness. The percentage of individuals reporting feeling lonely across age groups is even greater than that in southern Europe. The nations with the highest levels of loneliness were former Soviet states, including Ukraine, Russia, Hungary, Poland, etc. Yang and Victor therefore proposed that social change is closely associated with loneliness, as people were more likely to move away from their familiar social environments to somewhere else due to the political and economic changes since 1989. However, the mechanisms

underpinning this association along with the trajectories of loneliness in these nations need further examination.

Geography is another key issue that needs to be considered when tackling loneliness. It has been reported that in the UK, despite the unit cost of visiting a lonely person living in rural area being the same as visiting a lonely person living in an urban area, the time carers spend on the roads in rural areas is much more than in urban areas; this leads to a smaller amount of time being spent with lonely individuals living in rural areas than with those living in urban areas (Leggett, 2016). On a larger scale, geography is closely linked to social and cultural changes. Examples include national and international migrations. At national level, by investigating factors of loneliness among rural-to-urban migrants in Shanghai, Wen and Wang (2009) concluded that migrants often face social discrimination, have difficulties in adjusting to a new living and working environment, and have truncated social support networks, which leads to an excessive amount of social stress. At international level, based on the data from the Canadian General Social Survey, immigrants were found to be at greater risk of experiencing loneliness than their Canadian-born counterparts; this was more evident among those whose original cultures share neither the language nor similar social norms with Canadian (de Jong Gierveld et al., 2015).

Taken together, when developing preventative strategies and informing policies, in addition to targeting individual-level risk factors, it is also important to take the society level factors into account. Based on evidence discussed above, several interventions could be developed. For instance, in the UK and US, some promising results have been reported from intergenerational projects, e.g. day care within nursing homes, campus-affiliated retirement communities, intergenerational volunteering activities, as these projects provide elders more opportunities to interact with people, exchange their knowledge with youngers, etc. In the context of social and cultural change, providing language services and culture courses may help people, i.e. immigrants, familiarise themselves with the social rules and norms in their receiving countries, which might eventually benefit for building a better social relationship, developing a sense of security and belongings. Improving transportations may help people to maintain and strengthen their social relationships or build new

ones. A summary of the proposed ecological model targets on preventing and alleviating loneliness is listed in Figure 8.4.

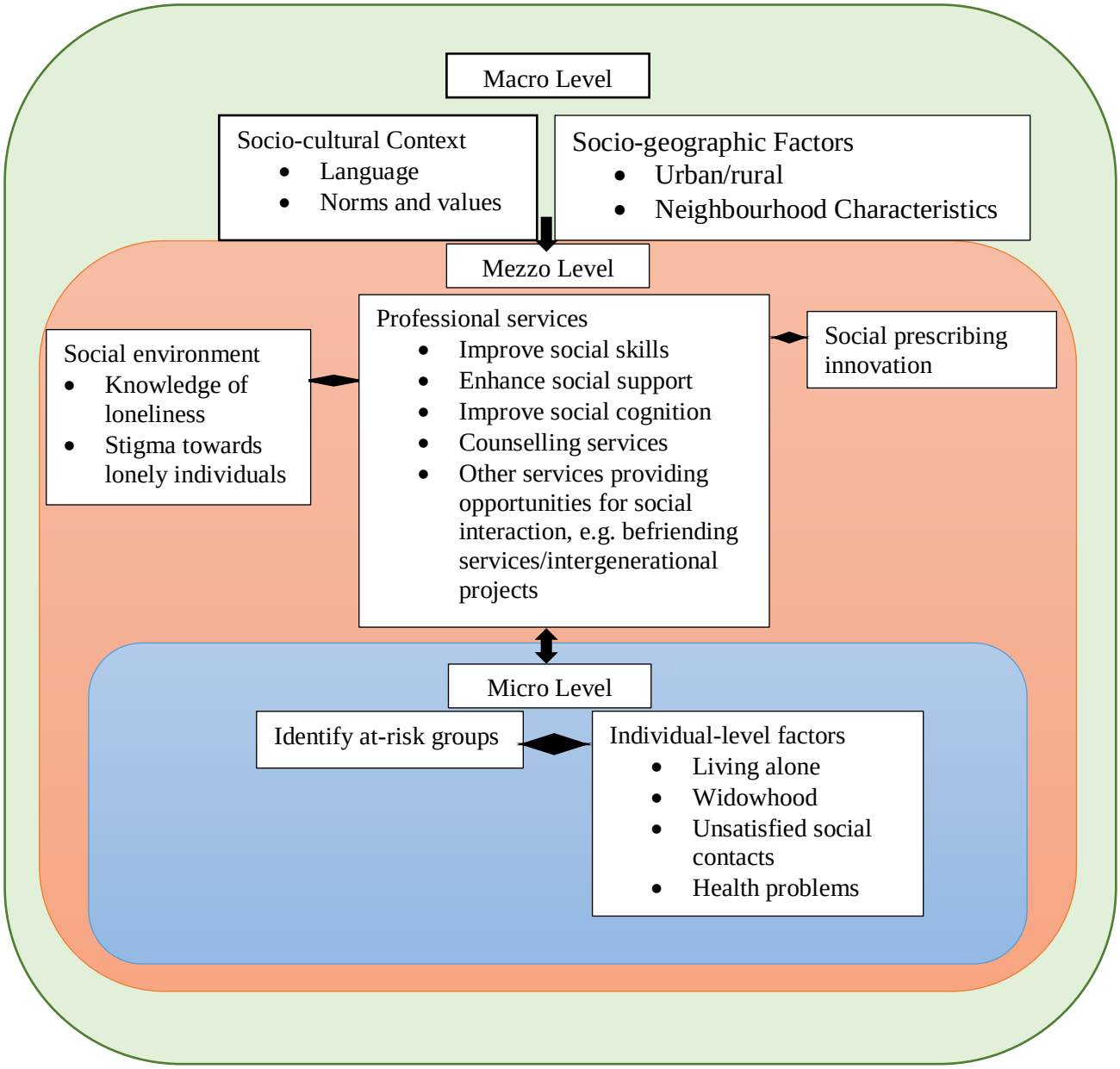


Figure 8. 4 The ecological framework for tackling loneliness

8.6 Future research direction

Since loneliness is an unpleasant, prevalent phenomenon (25% of individuals aged 65-79 suffer from loneliness and over 40% of individuals aged 80 and over experience loneliness) (Dykstra, 2009; mentioned in Chapter 2), preventing or alleviating loneliness is essential to improve well-being and quality of life and is clearly not only an individual's concern, but societies. Although an ecological approach to tackle loneliness is put forward in this thesis, empirical analyses only examined individual-level factors of loneliness. The potential influence of societal level factors, such as cultural, political and social values on loneliness, needs to be further investigated. To do so, data from national representative studies or multiple datasets with consistent measure of loneliness and other variables across countries need to be explored and analysed.

The determinants of loneliness may be different between men and women (Borys et al., 1985; Nicolaisen and Thorsen, 2014), and between those living in urban areas and rural areas (Havens et al., 2004). Gender variations within the oldest old population have not been explored to date, and cannot be tested in this thesis due to sample size. Consortia bringing together studies of the oldest old will be able to explore this issue.

Although multiple waves of data were used to explore the factors related to loneliness transitions, associations between loneliness and health outcomes, and between loneliness and health service and social care utilisation, the data only cover later life. Future work looking across life stages and different generations is important. This might be resolved by using data from existing appropriate epidemiological cohorts, such as the Medical Research Council National Survey of Health and Development (NSHD) (Ejlskov et al., 2017).

This thesis focuses on all-cause mortality and cognition as health outcomes. The non-significant findings between loneliness and mortality, and between loneliness and cognitive decline, suggest that loneliness was not a proximal risk factor for mortality and cognitive decline in the oldest old. Future research could address more specifically the association between loneliness and other health problems to explore

mechanisms underpinning the associations between loneliness, mortality and cognition. By doing so, a comprehensive view of the effects of loneliness on health can be generated.

According to the findings from the systematic review (Chapter 2), evidence on the association between loneliness and health service and social care utilisation were almost exclusively based on western countries. The evidence from eastern countries is limited. However, healthcare problems are rapidly increasing in these countries. For example, just like most countries across the world, China is facing rapid population ageing. The traditional social welfare system cannot meet the care needs resulting from the rapidly increased number of older people. The government has recognised the importance of community services and is prioritising fostering the development of community services (Zhou and Walker, 2016). Interestingly, in spite of the differences in social and cultural contexts, the specific services that the Chinese government focuses on are day care, dining rooms or other centralized meal delivery services, echoing the community services in western countries (Tian, 2010). Since the findings from Chapter 8 indicate a similar prevalence of loneliness in China and the UK (69% versus 73% feel occasionally lonely; 19% versus 10% feel always lonely in China and UK respectively), in order to achieve the maximum use of health and social care services, future studies in eastern countries need to investigate the impact of loneliness on health and social care service utilisation. Additionally, the findings from this thesis may shed light on service provision in eastern countries.

8.7 Conclusion

This thesis focuses on the exploration of loneliness in the oldest old. Specifically, the individual-level determinants of loneliness were investigated in cross-sectional and longitudinal analyses; the effects of loneliness on all-cause mortality and cognitive decline over time, as well as the association between loneliness and health service and social care utilisation were explored. Stressful life event (i.e. being widowed), negative experience (i.e. having poor quality of social connections), and physical and mental health decline (i.e. suffering from sight or hearing problems, depression) were found to be related to loneliness. In particular, a lower level of physical functioning and more severe depression were associated with increase in loneliness. The

identification of individual-level determinants of loneliness may shed light on the interventions that should be developed. Research focusing on investigating the mediators of the associations between loneliness and mortality and between loneliness and cognition could help better understand the underlying mechanisms. Although we have been aware for some time that chronic diseases, such as physical and cognitive impairments, are strong factors related to health and social care usage, loneliness as a risk factor has been neglected. Findings from the current study add new evidence to this end. In order to prevent or alleviate loneliness, the diversities of conceptualisations of loneliness, key determinants of loneliness, different contexts and settings need to be taken into account. Future research examining loneliness and its impact on health outcomes should be incorporated with a life course perspective and based on a larger context such as society level.

Appendices

Appendix 3.1 Computing cross-sectional weight for wave 3

3.1.1 Pathways through which eligible participants for wave 3 came

The wave 3 participants came from two pathways: (1) participated in wave 1 and wave 2, and (2) participated in wave 1 and Cambridge Mental Disorders of the Elderly Examination (CAMDEX 1) but did not participate in wave 2. In total, the number of (alive) participants at the time wave 2 completed were 1180 participants from pathway 1 and 317 from pathway 2 (Flowchart 3.1.1.1).

The eligibility criteria for participation in wave 3 was that the participants must be alive before the start of wave 3. Therefore, those who died after the completion of wave 2/CAMDEX1 study and before the start of wave 3 were excluded (N=336), this left 1161 (1180+317-336) participants as potentially eligible participants for wave 3. Of 1161 potentially eligible participants, 448 did not participate in wave 3. The reasons of not participating in wave 3 included (1) Not approached, (2) Too ill, (3) Died between the start and the end of wave 3 study, (4) Moved, not traceable, (5) Refused, and (6) Unknown reason. Table 3.1.1.1 gives the number of wave 3 non-participants under each specific reason.

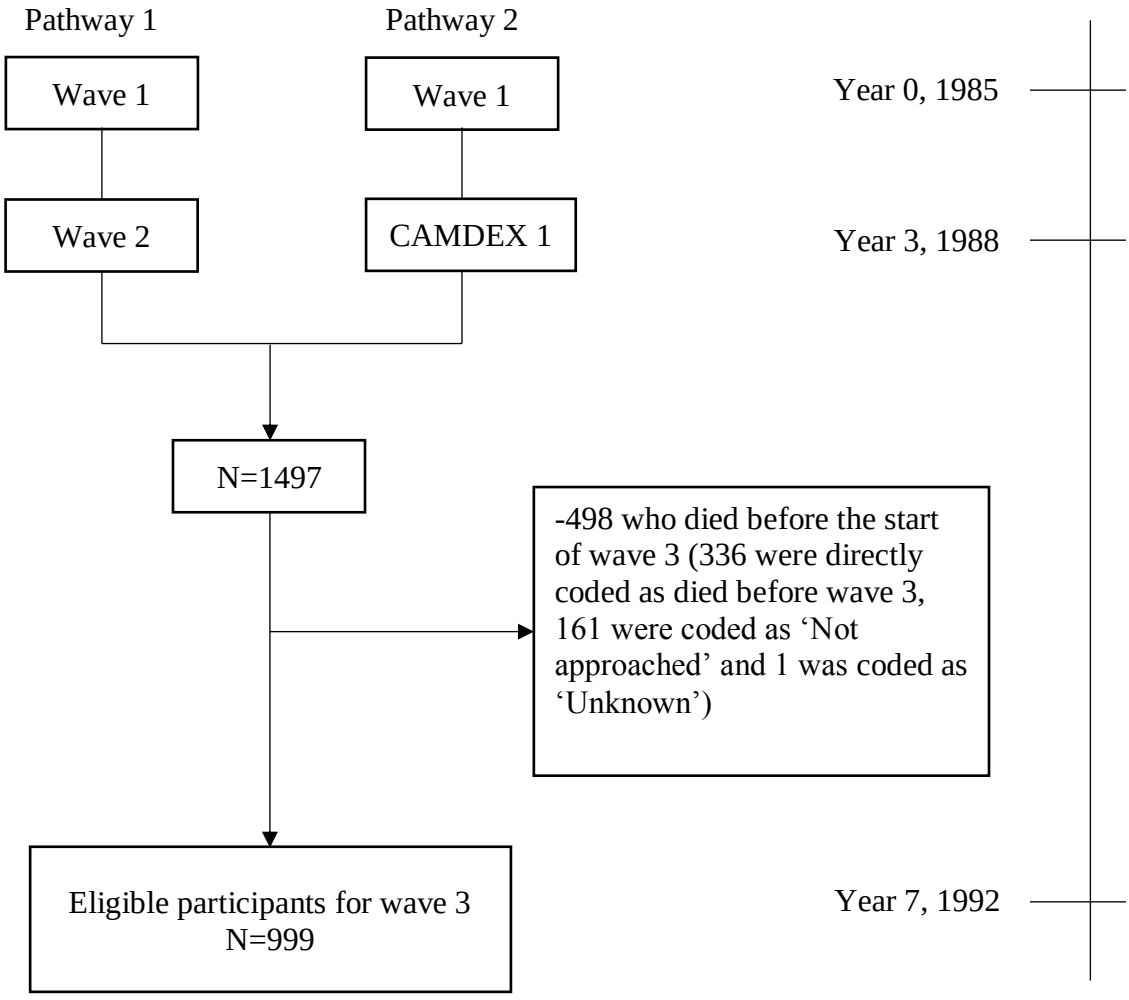
Table 3.1.1.1. Reasons and number of participants who were potentially eligible for wave 3 but did not participate in wave 3

	Not contacted		Contacted				
Reason	NA	M	Too ill	R	Unknown	Died during study*	Total
N	189	5	17	131	15	91	448

Note: NA: not approached; M: moved, not traceable; R: refused;
Died during study*: Died between the start and end of wave 3 study.

It should be noted that the non-response participants for wave 3 from category 'Not approached', 'Moved, not traceable' and 'Unknown' reasons might contain respondents who died before the start of wave 3. In order to avoid the inclusion of ineligible participants in later analyses, their death date was checked from death certificate records. After checking the death date, total 161 participants from category 'Not approached', and 1 participant from category 'Unknown' were further excluded

as they died before the start of wave 3. Therefore, the number of participants who were eligible for wave 3 was 999 (N=1161-161-1).



Flowchart 3.1.1.1 Pathways through which eligible participants for wave 3 came.

In addition, it should be noted that the participants from pathway 1 had different baseline characteristics from those from pathway 2. As stated in the CC75C cohort profile (Fleming et al., 2007), after wave 1, those who scored 23 or below and one in three of those who scored 24 or 25 in the Mini-Mental State Examination (MMSE) went to CAMDEX assessment; but they were excluded from wave 2 as the purpose of wave 2 was to detect the prevalence of incident dementia. However, from wave 3 and onwards, those who went to CAMDEX 1 (and were excluded from wave 2) were re-invited to the study in order to make the sample more representative of the population. Thus, although there were differences regarding cognitive ability between participants who participated in wave 1 and wave 2 and those who participated in wave 1 and CAMDEX 1, considering the study design (the purpose of wave 2) and the generalizability, I did not further test whether the wave 1 and wave 2 participants differed from wave 1 and CAMDEX 1 participants in terms of their baseline characteristics.

To conclude, the total number of eligible participants for wave 3 study was 999, of whom 872 were from pathway 1 and 127 were from pathway 2. In total, 713 participated in wave 3 and 286 did not.

3.1.2 Statistical methods to calculate cross-sectional weight

To calculate the stabilized inverse probability weight, logistic regression was used to calculate the numerator and the denominator. The numerator was the result of logistic regression with intercept only, and the denominator was the conditional probability of being exposed (i.e. participation in wave 3), which was estimated by fitting a logistic regression with a set of covariates. The dependent variable in both logistic regressions was an indicator with 0 indicating the non-participation and 1 reflecting participation in wave 3. The choice of covariates was based on previous studies (Austin and Stuart 2015; Lynn, 1996; Sadig 2014; Scholes et al., 2009, Xu et al., 2010); in this analysis, the covariates were age, sex, education, social class, self-rated physical health, cognitive function, physical functioning and route (indicator variable, 0=pathway 1, 1=pathway 2). The calculated weight is shown in Table 3.1.2.1.

Table 3.1.2.1. Distribution of cross-sectional weight for wave 3

	N	Mean	Std.dev	Min	Q1	Median	Q3	Max
Weight	713	1.00	0.46	0.76	0.86	0.89	0.97	4.49

Note: Std.dev: standard deviation; Q1: 25th percentile; Q3: 75th percentile.

According to Hernan & Robins (2017), the mean of the stabilized weight is expected to be 1, as the size of created pseudo-population reflects the size of the study population. Based on this, it can be concluded that the calculated weight was highly reasonable and therefore acceptable.

Appendix 4.1 Distribution of frequency of family and neighbour contacts at wave 3 (n=713)

	Frequency of family contact	Frequency of neighbour contact
	n (%)	
Weekly to none	357 (51.7%)	277 (41.7%)
At least 2-3 times a week	334 (48.3%)	387 (58.3%)

Appendix 4.2 Results from multivariable analyses included variable social class

	Multivariable analyses			
	A		B	
Risk factors	**OR**	**95% CI**	**OR**	**95% CI**
Age (85+)	1.0	0.7 - 1.5	-	-
Women	1.0	0.6 - 1.6	-	-
Length of widowhood (1 years)	**4.2**	**2.3 - 7.8**	-	-
Length of widowhood (over 1 years)	**2.4**	**1.4 - 4.3**	-	-
Live alone	**3.6**	**2.1 - 6.2**	-	-
Education (left school ≥15 years)	1.1	0.7 - 1.7	-	-
Social class (manual)	1.3	0.8 - 2.0		
Weekly to none contact with families	1.4	0.9 - 2.2	-	-
Weekly to none contact with neighbours	1.1	0.7 - 1.7	1.0	0.6 - 1.6
Unsatisfied with social contact	**2.5**	**1.6 – 3.9**	-	-
Lack of social engagement	1.2	0.8 - 1.8	-	-
Did not go out as much as like	**2.0**	**1.3 - 3.1**	-	-
Perceived good physical health	0.8	0.5 - 1.4	-	-
Perceived fair to poor physical health	0.9	0.5 - 1.7	-	-
Sight problems	**1.5**	**1.0 - 2.3**	-	-
Hearing problems	**1.5**	**1.0 - 2.3**	-	-
IADL disability	0.7	0.4 - 1.2	-	-
IADL and ADL disabilities	0.8	0.5 - 1.4	-	-
Depression	**4.3**	**2.3 – 8.0**	-	-

Note: (1) OR: odds ratio; 95% CI: 95% confidence interval; (2) reference groups by order: age (80-84), men, not widowed, live with others, education (left school <15 years), social class (non-manual), frequency of family contact (at least 2-3 times a week), frequency of neighbour contact (at least 2-3 times a week), feeling satisfied with social contact, engaged in at least one social activity, went out as much as like, perceived very good physical health, did not have sight problems, did not have hearing problems, not disabled and not depressed (2) A: (lonely, slightly lonely) vs. not lonely; B: lonely vs. (slightly lonely, not lonely); '-': indicates same effect size.

Appendix 4.3 Results from sensitivity analyses adjusting for missing data in independent variables

	Analysis with imputed data				Worst case analysis			
	A		B		A		B	
Risk factors	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age (85+)	1.0	0.7 - 1.5	-	-	1.0	0.7 - 1.5	-	-
Women	1.0	0.6 - 1.6	-	-	1.0	0.6 - 1.6	-	-
Length of widowhood (1 year)	**4.2**	**2.2 - 7.7**	-	-	**4.6**	**2.5 - 8.3**	-	-
Length of widowhood (over 1 year)	**2.4**	**1.4 - 4.3**	-	-	**2.5**	**1.4 - 4.3**	-	-
Live alone	**3.6**	**2.1 - 6.1**	-	-	**3.2**	**1.9 - 5.2**	-	-
Education (left school >=15 years)	1.2	0.8 - 1.8	-	-	1.2	0.9 - 1.8	-	-
Weekly to no contact with families	1.4	0.9 - 2.2	-	-	1.4	0.9 - 2.0	-	-
Weekly to no contact with neighbours	1.1	0.7 - 1.7	1.0	0.6 - 1.6	1.0	0.7 - 1.5	-	-
Unsatisfied with social contact	**2.6**	**1.6 - 4.0**	-	-	**2.7**	**1.8 - 4.1**	-	-
Lack of social engagement	1.2	0.8 - 1.8	-	-	1.2	0.8 - 1.8	-	-
Did not go out as much as like	**2.0**	**1.3 - 3.0**	-	-	**2.0**	**1.3 – 3.1**	-	-
Perceived good physical health	0.8	0.5 - 1.3	-	-	0.9	0.6 - 1.3	-	-
Perceived fair to poor physical health	0.9	0.5 - 1.6	-	-	0.9	0.6 - 1.5	-	-
Sight problems	**1.5**	**1.0 - 2.3**	-	-	**1.6**	**1.1 - 2.4**	-	-
Hearing problems	**1.5**	**1.1 - 2.3**	-	-	**1.6**	**1.1 - 2.3**	-	-
IADL disability	0.7	0.4 - 1.2	-	-	0.7	0.4 - 1.2	-	-
IADL and ADL disabilities	0.8	0.5 - 1.3	-	-	0.8	0.5 - 1.3	-	-
Depression	**4.3**	**2.3 - 7.9**	-	-	**2.3**	**1.4 - 3.9**	-	-

Note: A: (lonely, slightly lonely) vs. non-lonely; B: lonely vs. (slightly lonely, non-lonely).

Appendix 4.4 Distribution of wave 3 loneliness according to wave 4 participation

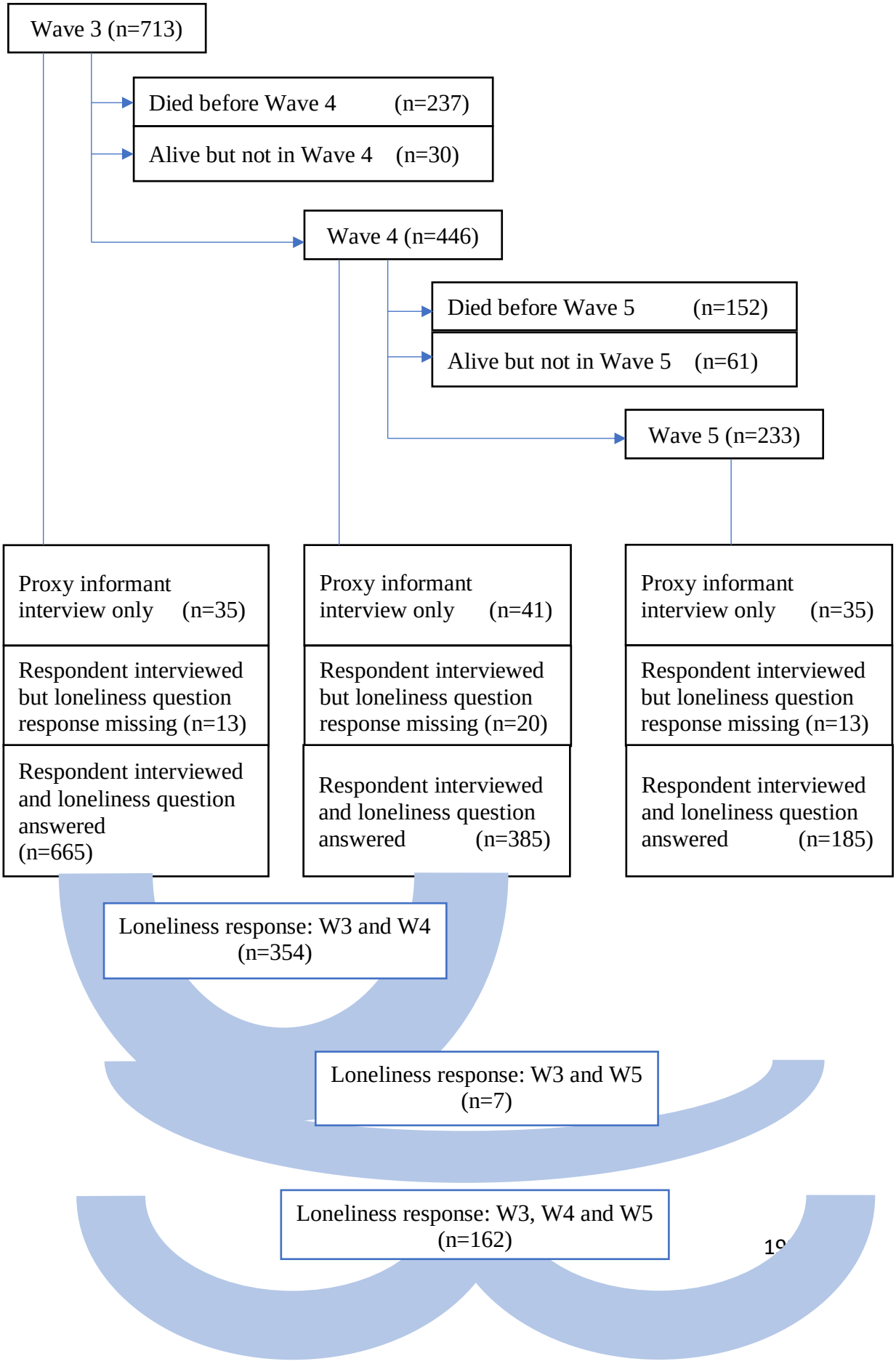
			Dropout			
% (N)	Total	In wave 4	Other*	Refused+	Died	Chi-2 p-value
Not lonely	59.0 (392)	60.3 (232)	43.3 (13)	66.7 (24)	57.8 (123)	
Slightly lonely	16.1 (107)	16.9 (65)	23.3 (7)	13.9 (5)	14.1 (30)	0.38
Lonely	24.9 (165)	22.9 (88)	33.3 (10)	19.4 (7)	28.2 (60)	

Appendix 4.4 cont. Distribution of wave 4 loneliness according to wave 5 participation

			Dropout			
%(N)	Total	In wave 5	Other*	Refused+	Died	Chi-2 p-value
Not lonely	60.3 (232)	59.7 (117)	73.9 (17)	66.7 (16)	57.8 (82)	
Slightly lonely	16.9 (65)	19.9 (39)	8.7 (2)	16.7 (4)	14.1 (20)	0.36
Lonely	22.9 (88)	20.4 (40)	17.4 (4)	16.7 (4)	28.2 (40)	

Note: Other*: including not approached, unknown reason, moved away from study area, other reason; Refused+: including refusal, refusal by relative, refusal at telephone contact, refusal at door, permanent refusal, too ill to take part.

Appendix 5.1 Loneliness non-response at wave 3, wave 4 and wave 5



Appendix 5.2 Participants' characteristics were compared according to the missingness of loneliness at wave 4 and wave 5

	No missing data on loneliness [A] (W3, W4 or W5)	Missing data on loneliness at one wave [B] (either W4 or W5)	Missing data on loneliness at two waves [C] (both W4 and W5)	Chi-2 p-value
	n=484	n=157	n=24	
Age				
80-84	45	45	54	0.698
85+	55	55	46	
Sex				
Men	32	31	25	0.780
Women	68	69	75	
Residence				
House/flat/granny flat	79	81	79	0.538
Warden controlled	11	12	17	
Residential home/hospital	10	7	4	
Marital status				
Married	24	28	13	0.639
Widowed	63	62	67	
Separated/divorced	2	2	4	
Single	10	8	17	
Education				
Left school < 15 years	63	64	54	0.858
Left school >= 15 years	36	36	46	
Missing	1	0	0	
Social class				
Manual	57	57	63	0.943
Non-manual	41	41	37	
Missing	2	2	0	
Cognition				
Normal cognition	43	32	17	<.05
Mild CI+	27	33	33	
Moderate CI+	15	17	25	
Severe CI+	13	14	17	
Missing	1	4	8	

Number of chronic diseases				
0-2	61	64	54	0.838
≥ 3	35	31	42	
Missing	4	5	4	
Physical functioning				
No disability	36	39	50	0.604
IADL disability	26	29	21	
IADL and ADL disability	37	30	29	
Missing	1	2	0	
Depression				
No	80	86	79	0.201
Yes	13	7	8	
Missing	7	7	13	
Loneliness (wave 3)				
Not lonely	58	63	50	0.575
Slightly lonely	17	13	25	
Lonely	25	24	25	

Note: A: individuals who self-reported loneliness as long as they were alive; B: individuals who did not report loneliness at either wave 4 or wave 5 but known alive; C: individuals who did not report loneliness at both wave 4 and wave 5 but known alive; CI^+: cognitive impairment; Participants' cognitive function was assessed by Mini-Mental State Examination, the total score ranges from 0-30, and categorized as normal cognition (score 26-30), mild cognitive impairment (score 22-25), moderate cognitive impairment (score 18-21) and severe cognitive impairment (score 0-17) (Folstein et al., 1975).

Appendix 5.3 Sensitivity analysis to test the potential influence of follow-up length on the association between loneliness and mortality risk: Five-year mortality risk of loneliness

	Model 1		Model 2		Model 3	
	HR	95% CI	HR	95% CI	HR	95% CI
Not lonely	1.0	-	1.0	-	1.0	-
Slightly lonely	0.9	0.7 - 1.2	0.9	0.7 - 1.2	0.9	0.7 - 1.2
Lonely	1.3	1.1 - 1.6	1.2	1.0 - 1.5	1.1	0.9 - 1.4

Note: HR: hazard ratio, 95% CI: 95% confidence interval.

Model 1: adjusted for age, sex, residential type, marital status and education.

Model 2: Model 1 further adjusted for number of chronic diseases and physical functioning.

Model 3: Model 2 further adjusted for depression.

Appendix 5.4 Sensitivity analysis excluding 57 participants who died within one year from when their initial loneliness levels were recorded

	Model 1		Model 2		Model 3	
	HR	95% CI	HR	95% CI	HR	95% CI
Not lonely	1.0	-	1.0	-	1.0	-
Slightly lonely	0.9	0.7 - 1.3	0.9	0.6 - 1.2	0.9	0.7 - 1.2
Lonely	1.3	1.0 - 1.7	1.2	0.9 - 1.6	1.1	0.8 - 1.5

Note: HR: hazard ratio, 95% CI: 95% confidence interval.

Model 1: adjusted for age, sex, residential type, marital status and education.

Model 2: Model 1 further adjusted for number of chronic diseases and physical functioning.

Model 3: Model 2 further adjusted for depression.

Appendix 5.5 Sensitivity analysis to test the potential bias due to left-truncation

	Model 1		Model 2		Model 3	
	HR	95% CI	HR	95% CI	HR	95% CI
Not lonely	1.0	-	1.0	-	1.0	-
Slightly lonely	0.9	0.7 - 1.3	0.9	0.7 - 1.2	0.9	0.7 - 1.2
Lonely	1.2	1.0 - 1.6	1.1	0.9 - 1.5	1.0	0.8 - 1.4

Note: HR: hazard ratio, 95% CI: 95% confidence interval.

Model 1: adjusted for age, sex, residential type, marital status and education.

Model 2: Model 1 further adjusted for number of chronic diseases and physical functioning.

Model 3: Model 2 further adjusted for depression.

Appendix 6.1 Factors associated with lack of MMSE score at wave 3

	OR	95% CI
Age	0.94	0.86-1.01
Sex	0.63	0.29-1.39
Education	1.10	0.50-2.40
IADL disability	0.57	0.14-2.22
ADL and IADL disability	0.09	0.03-0.27

Results shown in the table were from logistic regression
OR: odds ratio; 95% CI: 95% confidence interval
Age was treated as continuous variable, references for other variables by order were: men, left school ≥15, and no disabilities
MMSE: Mini Mental State Examination
IADL: Instrumental Activities of Daily Living
ADL: Activities of Daily Living

Appendix 6.2 Factors associated with dropping out, excluding mortality, during follow-up

	Dropout at wave 4		Dropout at wave 5		Dropout at wave 6		Dropout at wave 7	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Age*	1.09	1.03-1.16	1.05	0.92-1.19	1.51	0.89-2.57	1.16	0.63-2.11
Sex	0.67	0.47-0.96	0.56	0.27-1.14	0.30	0.04-2.44	0.14	0.01-1.79
Education (left school <15)	1.18	0.83-1.68	1.66	0.81-3.40	0.18	0.03-1.14	0.31	0.02-4.20
MMSE*	0.89	0.85-0.92	0.87	0.82-0.93	0.82	0.67-0.99	0.96	0.79-1.16

* indicates variables, age and MMSE, were measured at previous wave.

In logistic regression, age and MMSE scores were treated as continuous variables, references for sex and education were men and left school ≥ 15, respectively.

Appendix 6.3 Number of participants with valid MMSE scores and responses to lonely questions, and the percentage of missingness of loneliness

	Valid MMSE score	Having data on loneliness	Missingness of loneliness*
	n	n	(%)
wave 3	657	651	9
wave 4	351	339	3
wave 5	160	154	4
wave 6	55	51	7
wave 7	18	14	22
wave 8	10	9	10
wave 9	3	2	33
wave 10	1	1	0

Missingness of loneliness* was defined as individuals who did not report loneliness but had valid MMSE score.

Appendix 6.4 The impact of time-varying loneliness on cognitive function decline adjusting for MMSE and loneliness missingness

	Coefficient	**95% CI**
Loneliness level		
Slightly lonely	-0.8	(-2.6, 1.1)
Lonely	-0.3	(-1.8, 1.2)
Age		
85-89 (at wave 3)	-2.4	(-4.3, -0.6)
90+ (at wave 3)	-7.6	(-12.4, -2.8)
Time	0.9	(-3.3, 5.1)
Sex		
Women	-0.1	(-1.7, 1.7)
Women x Time	-2.0	(-4.3, 0.4)
Education		
Left school <15 years	-2.5	(-3.8, -1.2)
Left school <15 years x Time	0.2	(-1.1, 1.5)

Note: references groups: not lonely, aged 80-84 at wave 3, men, left school ≥15 years. Time: number of years since wave 3.

Appendix 7.1 Associations between baseline loneliness and health and social care utilisation (results from analysis with the original coding of 'time since last saw a GP')

	Home Help	**Community Nurse**	**Meals on Wheels**	**Day centre**	**Hospital visits**	**Time since last saw a GP**
	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	Beta (95% CI)
Time	1.1 (0.4-2.8)	2.5 (0.9-6.9)	1.1 (0.4-2.8)	0.9 (0.3-2.6)	1.5 (0.7-3.0)	0.1 (-0.3, 0.6)
Loneliness (wave 3)						
Slightly lonely	1.3 (0.5-3.6)	0.6 (0.2-2.2)	1.9 (0.8-4.9)	1.6 (0.5-5.0)	1.3 (0.8-2.1)	**-0.5 (-0.8, -0.2)**
Lonely	2.4 (0.8-7.3)	1.1 (0.5-2.5)	2.0 (0.9-4.5)	1.4 (0.3-5.3)	1.2 (0.8-1.9)	-0.1 (-0.5, 0.3)
Age						
85-89	0.5 (0.2-1.1)	0.8 (0.4-1.9)	0.8 (0.4-1.7)	1.0 (0.4-2.3)	0.7 (0.5-1.1)	0.2 (-0.1, 0.5)
90+	0.9 (0.2-3.9)	0.9 (0.3-2.6)	0.6 (0.1-3.6)	1.6 (0.1-19.9)	1.3 (0.6-2.9)	0.02 (-0.6, 0.7)
Sex						
Women	1.3 (0.5-3.2)	0.7 (0.3-2.0)	0.8 (0.4-2.0)	1.4 (0.6-3.4)	0.7 (0.4-1.1)	**-0.5 (-0.8, -0.1)**
Physical impairments						
Moderate	**2.3 (0.96-5.4)**	2.2 (0.9-5.1)	0.6 (0.2-1.5)	1.6 (0.4-5.8)	1.3 (0.8-2.1)	-0.2 (-0.5, 0.2)
High	**3.9 (1.5-10.6)**	2.0 (0.8-5.1)	1.9 (0.8-4.6)	3.2 (0.7-13.6)	**2.5 (1.4-4.6)**	-0.3 (-0.7, 0.1)
Health condition						
≥ 3	1.5 (0.7-3.3)	**2.4 (1.1-5.0)**	1.2 (0.6-2.5)	2.1 (0.7-6.5)	1.1 (0.7-1.7)	**-0.3 (-0.6, -0.1)**
Depression						
Yes	0.6 (0.2-1.6)	0.6 (0.2-1.9)	0.5 (0.2-1.5)	**0.3 (0.1-1.0)**	1.1 (0.5-2.2)	**-0.4 (-0.8, -0.1)**
Physical functioning						
IADL disability only	2.4 (0.9-6.4)	1.0 (0.3-3.2)	0.8 (0.3-2.6)	2.4 (0.9-6.3)	0.7 (0.4-1.2)	-0.3 (-0.7, 0.1)
IADL & ADL disabilities	2.3 (0.9-6.2)	1.6 (0.6-3.9)	1.5 (0.6-3.7)	**2.9 (0.96-8.9)**	1.0 (0.6-1.7)	0.1 (-0.2, 0.4)
Cognition	0.9 (0.8-1.1)	1.0 (0.9-1.1)	0.9 (0.8-1.1)	1.0 (0.8-1.1)	1.0 (0.9-1.1)	-0.05 (-0.1, 0.01)

Reference groups: not lonely, 80-84 years old, men, no physical impairments, 0-2 chronic diseases, not depressed, and not disabled.
IRR: incidence rate ratio. Beta: regression coefficient.

Appendix 7.2 Associations between time-varying loneliness and health and social care utilisation (results from analysis with original coding of 'time since last saw a GP')

	Home Help	**Community Nurse**	**Meals on Wheels**	**Day centre**	**Hospital visits**	**Time since last saw a GP**
	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	IRR (95% CI)	Beta (95% CI)
Time	1.0 (0.4, 2.5)	2.3 (0.9, 5.8)	1.0 (0.4, 2.6)	1.4 (0.4, 4.9)	1.3 (0.7, 2.6)	0.1 (-0.3, 0.5)
Loneliness						
Slightly lonely	1.2 (0.5, 2.9)	0.8 (0.3, 2.6)	1.6 (0.6, 3.8)	1.7 (0.5, 5.5)	1.4 (0.9, 2.1)	-0.3 (-0.6, 0.1)
Lonely	2.0 (0.8, 4.9)	**3.4 (1.4, 8.7)**	**2.5 (1.1, 5.6)**	1.4 (0.4, 5.3)	1.5 (0.9, 2.4)	-0.2 (-0.5, 0.1)
Age						
85-89	0.5 (0.2, 1.1)	0.8 (0.3, 1.9)	1.0 (0.5, 2.0)	1.0 (0.4, 2.5)	0.7 (0.5, 1.2)	0.2 (-0.1, 0.5)
90+	0.9 (0.2, 4.4)	1.3 (0.4, 4.7)	0.6 (0.1, 5.9)	4.2 (0.3, 51.7)	1.0 (0.4, 2.7)	0.1 (-0.6, 0.7)
Sex						
Women	1.2 (0.5, 3.1)	0.5 (0.2, 1.5)	0.8 (0.3, 1.9)	1.4 (0.5, 4.0)	**0.6 (0.4, 1.002)**	**-0.5 (-0.9, -0.2)**
Physical impairments						
Moderate	2.3 (0.9, 5.7)	1.9 (0.8, 4.5)	0.7 (0.2, 2.0)	4.0 (0.7, 23.4)	1.3 (0.8, 2.1)	-0.1 (-0.5, 0.2)
High	**4.1 (1.6, 10.8)**	1.4 (0.4, 4.5)	1.9 (0.7, 5.3)	**7.6 (1.2, 48.7)**	**2.3 (1.2, 4.4)**	-0.3 (-0.7, 0.1)
Health condition						
≥3	1.5 (0.7, 3.3)	**2.6 (1.2, 5.5)**	1.2 (0.6, 2.6)	2.3 (0.6, 8.7)	1.2 (0.8, 1.9)	**-0.3 (-0.6, -0.1)**
Depression						
Yes	0.6 (0.2, 1.6)	0.5 (0.2, 1.5)	0.5 (0.2, 1.7)	0.3 (0.1, 1.1)	1.1 (0.5, 2.1)	**-0.4 (-0.8, -0.03)**
Physical functioning						
IADL disability only	2.1 (0.8, 5.6)	0.9 (0.3, 2.7)	0.8 (0.2, 2.6)	2.7 (0.9, 8.5)	0.7 (0.4, 1.3)	-0.3 (-0.7, 0.1)
IADL & ADL disabilities	2.3 (0.8, 6.3)	1.0 (0.4, 2.5)	1.5 (0.5, 4.5)	2.1 (0.7, 6.7)	1.0 (0.6, 1.7)	0.2 (-0.1, 0.5)
Cognition	0.9 (0.8, 1.0)	0.9 (0.8, 1.0)	0.9 (0.8, 1.1)	1.1 (0.9, 1.2)	1.0 (0.9, 1.1)	-0.05 (-0.1, 0.0003)

Reference groups: not lonely, 80-84 years old, men, no physical impairments, 0-2 chronic diseases, not depressed, and not disabled.
IRR: incidence rate ratio. Beta: regression coefficient.

Appendix Side Project

Cross-cultural perspectives of loneliness

1. Project Overview

In previous chapters, the determinants of loneliness and loneliness as a risk factor for all-cause mortality, cognition and health service and social care utilisation were investigated. Loneliness was measured via single-item question "Do you feel lonely?", which implies that all the participants have a common understanding of loneliness. Moreover, as for other measurements in this research area, such as UCLA Loneliness Scale, de Jong Gierveld Loneliness Scale, assess loneliness exclusively from researchers' perspective (i.e. questions used were conceptualised by researchers, though they might rely on self-reported responses). As mentioned in Chapter 1 (Section 1.4), scientific research should generate findings that are relevant to population being studied. In addition, exploring laypeople's perception of cultural and geographic diversity would help achieve a fuller view of the research questions being studied. Thus far, only one qualitative study has been conducted to explore how laypeople describe loneliness. This study was based on a limited number of older participants (30 older Norwegians, aged 70-97 years) (Hauge and Kirkevold, 2010). Studies investigating lay perspectives of loneliness in more than one culture have not been conducted. Furthermore, perceptions of loneliness among different age groups has received a little attention. The current chapter explores perspectives of laypeople aged 18 and over from the UK and China.

2. Introduction

Although there is no clear and consistent conceptualisation of loneliness in the classical research literature, loneliness is commonly understood as an abnormal, painful experience that is associated with one's social relationships. However, as reported in Chapter 1, different researchers may conceptualise loneliness from different approaches and categorise it into different dimensions; the assessment tools for measuring loneliness differ across studies as well. Although these researcher-driven conceptualisations of and the assessments of loneliness are widely used, the questions asked in the assessments focus on different aspects (Figure S.1), inhibiting cross-study comparisons. More importantly, without the explicit input of laypeople's perspectives of loneliness (laypeople refers to individuals who do not have professional or specialised knowledge of loneliness), it is impossible to develop a comprehensive understanding of loneliness. Furthermore, exploring the ways in which loneliness is articulated by laypeople in everyday language may help policy makers and researchers to develop or tailor existing resources and policies to prevent or alleviate loneliness.

To date, there is only one study investigating how people describe loneliness as well as how they cope with it; however, the study has a small scale with 30 participants aged over 70 years old, and is based in Norway (Hauge and Kirkevold, 2010). Furthermore, previous studies have found that loneliness is associated with social stigma, and is often linked to shame, guilt and frustration (de Jong Gierveld, 1998). Moreover, the current interventions do not produce promising results (Cattan et al., 2005; Masi et al., 2011). On the other hand, the idea of implementing artificial intelligence (AI) in healthcare is on the rise. Artificial intelligence (AI) has great potential to assist with day-to-day tasks that are difficult to perform by individuals with health problems. Social robots are being developed around the world, including those that can provide companionship and offer a platform for social interaction for older people (e.g. Broekens et al., 2009). Therefore, there is a great potential for implementing AI as a prevention or intervention tool to help with loneliness, an area worth exploring.

A one-child policy has been in place in China since the late 1970s. It created a unique social phenomenon – *"Shidu"* (refers to parents who lost their only child). It is

reported that the total number of *"Shidu"* families who have lost their adult child (aged over 30) is approximately 1 million, and the number is doubled if counting the death of only children who were aged under 15 (Song, 2014). Since the parent-child bond is emphasised in Chinese tradition over thousands of years, the impact of losing an only child on a family is devastating (as it is to all such parents). Previous research found that *"Shidu"* parents are more likely to feel lonely than their counterparts, and this becomes more prominent during festivals, the special occasions when the whole family is expected to reunite together (Jiang, 2015). The one-child policy was relaxed in 2016, however, to date there has been no study investigating the potential impact of the new policy (i.e. relaxed one-child policy) on individuals' health (including feelings of loneliness).

Taken together, the current study aims to investigate lay perspectives of loneliness in the UK and China by exploring how they conceptualise it or whether different domains of loneliness are emphasized in different cultures, what strategies they use to cope with it, what specific bias or criticisms lonely individuals encounter, how they accept the idea of AI as a prevention or intervention tool, as well as how respondents from China think the new relaxed one-child policy will impact experience of loneliness. Countries were chosen based on the native languages of the researchers.

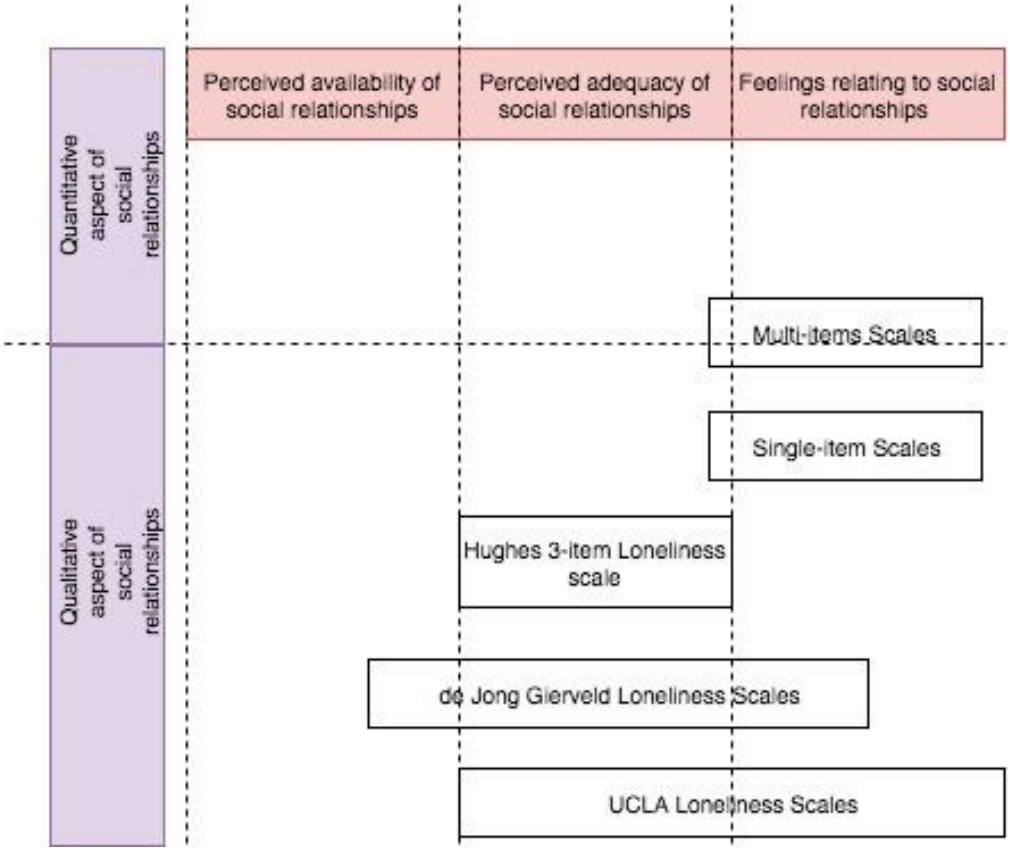


Figure S. 1 The comparisons of instruments used to assess loneliness in current research literature

Adapted from "Loneliness, social isolation and social relationships: what are we measuring? A novel framework for classifying and comparing tools" (Valtorta et al., 2016).

Note: examples of the most commonly used single-item scales: "How often do you feel lonely?", "Do you feel lonely?" or "How frequently have you felt lonely over the past week?". Depending on studies, the single-item scales and multiple-item scales may be used to measure loneliness experienced in past or present.

3. Methods

3.1 Respondents

To be eligible for this study, respondents had to be a national of the UK or China, and aged 18 years or over.

3.2 Design and sampling

A semi-structured survey (i.e. consisting of both closed and open-ended questions) was developed to learn about laypeople's understanding of loneliness. The use of open-ended questions, for example, "What is your experience of loneliness? Please use a few sentences to describe the feeling" is to make sure the answers given by respondents are based on their own feelings or knowledge. Questions covered a wide range of domains from the conceptualisation of loneliness, coping strategies, to the acceptability of artificial intelligence as a potential tool to help with preventing or alleviating loneliness; basic demographic information was also collected, such as age, sex, marital status, education. The survey was developed in both English and Chinese by a bilingual speaker (HW) whose native language is Chinese; the English version was proof-read by the principal investigator (CB) and the Chinese version was proof-read by another bilingual speaker (ZY). The proof-reading was to ensure the contents written in two languages were consistent and cohesive. Any discrepancies were resolved through discussion. The Chinese version included an extra question regarding people's attitudes towards the relationship between relaxed one-child policy and loneliness. The survey took approximately 15 minutes to complete.

The survey was anonymous and self-administered via the online survey platform SmartSurvey (https://www.smartsurvey.co.uk/). In order to distribute the surveys and to reach as many potential respondents as possible, the snowball method was applied through social networking sites, notably Facebook in UK and Wechat in China. Snowball sampling is a technique where existing research subjects recruit future subjects through their social networks (Biernacki et al., 1981). Facebook is the most popular social network site across the world; the estimated number of active users was 2,234 million in April 2018. Wechat is the leading social media site in China with more than 980 million active users per month (www.statista.com, 2018).

Apart from online social network sites, researchers' personal social networks were utilised (e.g. through email contact) to distribute survey links.

3.3 Ethical issues and approval

Upon clicking the survey link, respondents were not immediately directly exposed to research questions, but were provided with detailed information on the current study, including research aims and objectives, and were asked to give their informed consent (Appendix 8.1). Only after this, respondents could progress to the survey questions. There were 14 questions (15 in the Chinese version), each question was mandatory, respondents had to answer each of them to continue to the next question. In order to ensure the respondent's right to decide which questions they would like to answer, an option *Prefer not to say* was listed for each closed question and *Not Applicable* for each open-ended question (Appendix 8.2). Respondents could terminate answering the survey at any stage. This study was approved by the Psychology Research Committee of the University of Cambridge (application reference Pre.2017.099, approval date: 14th December, 2017).

3.4 Data analysis

Data were exported from the online platform SmartSurvey into a Word document. Trustworthiness of the translation is most important when collecting qualitative data in one language and presenting them in another. To ensure the trustworthiness and reliability of the data, the most common procedure is to translate the source data into the target version and back-translate the target version into source data. Since the quality of translation is determined by the linguistic competence of the translator and the translator's knowledge of the people under study, the recommended way to do translation and back-translation is to involve one bilingual researcher who is familiar with the people under study and another bilingual researcher who is familiar with the research subject (Birbili, 2000; Chen and Boore, 2010). Therefore, before the initial coding, responses written in Chinese were translated to English by HW (a bilingual Chinese and English speaker who is familiar with the study subject). The translation was double-checked by another researcher ZY (a bilingual Chinese and English speaker) to address any translational issues and to ensure that any nuances were best captured. Any discrepancies were resolved through discussion. Then HW back-

translated the English version to Chinese to evaluate the equivalence between the original Chinese version and the translated English version. The final English version was then uploaded into Nvivo 12 for further analysis. Nvivo is a qualitative data analysis software tool (QSR International Pty Ltd, version 12, 2018). The procedure of translation and back-translation is illustrated in Figure S.2.

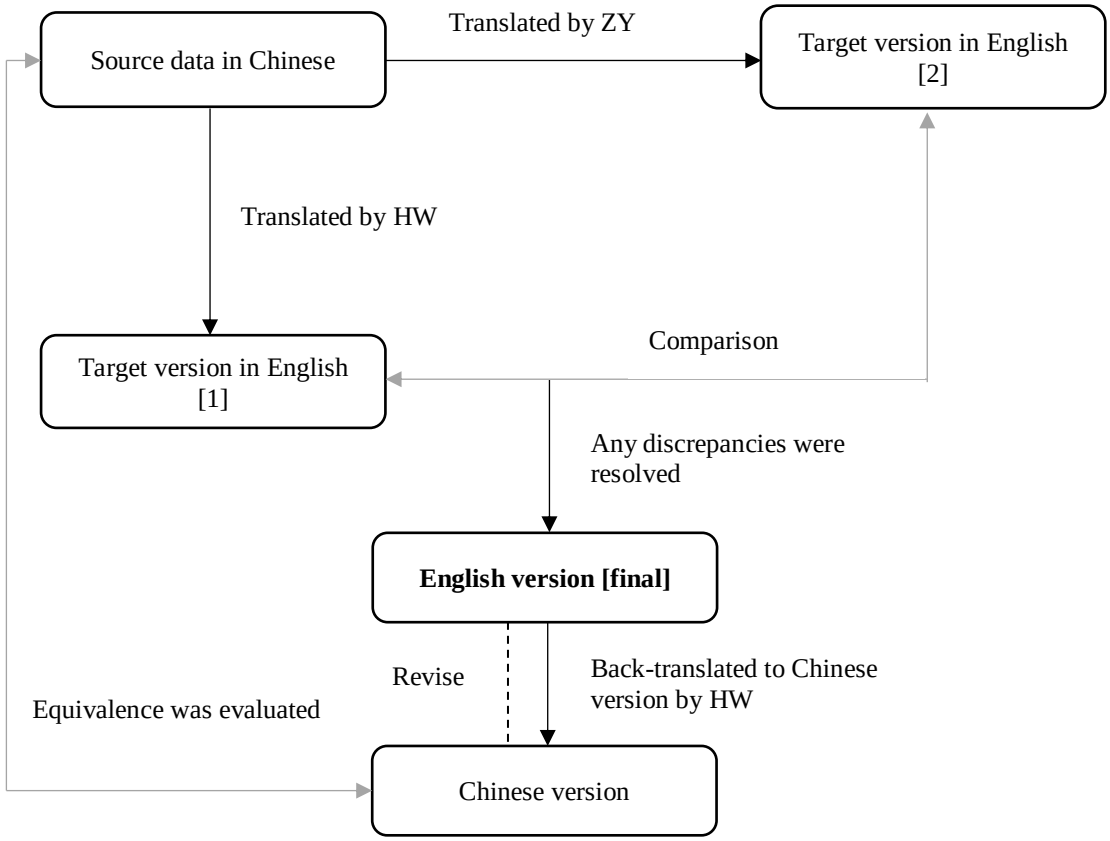


Figure S.2 Translation and back-translation procedures

The open-ended questions were analysed by using thematic analysis method. Thematic analysis is a flexible qualitative study method aimed to identify, analyse and report themes within research data. It focuses on patterning of meaning across responses and generating insights into the data. Six analysing phases were involved in thematic analysis including familiarisation with data, generating initial codes, searching for themes, reviewing themes, defining and naming themes and producing the report (Braun and Clarke, 2006). The current analysis was conducted step-by-step by following these guidelines (Table S.1), and implemented in Nvivo 12.

Table S. 1 Analysing phases of thematic analysis

Phase	Description of the process	Analyse procedure
1. Familiarisation with data	Transcribing data (if necessary), reading and re-reading the data, noting down initial ideas.	HW read through all the responses three times to be familiar with the data. During reading process, HW paid attention to searching for main themes to each research question.
2. Generating initial codes	Coding interesting features of the data in a systematic fashion across the entire data set, collating data relevant to each code.	HW re-read all responses and generated codes to label the features of the data.
3. Searching for themes	Collating codes into potential themes, gathering all data relevant to each potential theme.	Themes were developed through the first two phases; the responses were then collated under each corresponding theme.
4. Reviewing themes	Checking if the themes work in relation to the coded extracts (Level 1) and the entire data set (Level 2), generating a thematic 'map' of the analysis.	The first three steps were repeated to ensure all relevant features of responses were captured and categorised into corresponding themes.
5. Defining and naming themes	Ongoing analysis to refine the specifics of each theme, and the overall story the analysis tells, generating clear definitions and names for each theme.	The codes and themes were further refined during analysis.
6. Producing the report	The final opportunity for analysis. Selection of vivid, compelling extract examples, final analysis of selected extracts, relating back of the analysis to the research question and literature, producing a scholarly report of the analysis.	Report was produced in accordance with the criteria.

Note: Table was adapted from *"Using thematic analysis in psychology" by Braun and Clarke, 2006.*

4. Results

4.1 Respondent characteristics

Total 238 responses were collected (British: 58; Chinese: 180). Individuals aged between 25 and 34 made up the largest proportion of total respondents. Primarily they were women, married, left school after 16 years old, feeling occasionally lonely (Table S.2).

Table S. 2 Description of respondents' characteristics by country

Country	UK n=58	China n=180	Total n=238
% (n)			
Age			
18-24	29 (n=17)	15 (n=27)	18 (n=44)
25-34	36 (n=21)	39 (n=71)	39 (n=92)
35-44	12 (n=7)	13 (n=24)	13 (n=31)
45-54	19 (n=11)	28 (n=50)	26 (n=61)
55-64	2 (n=1)	3 (n=6)	3 (n=7)
65-74	2 (n=1)	0 (n=0)	0.4 (n=1)
75+	0 (n=0)	1 (n=1)	0.4 (n=1)
Prefer not to say	0 (n=0)	1 (n=1)	0.4 (n=1)
Sex			
Male	26 (n=15)	43 (n=77)	39 (n=92)
Female	74 (n=43)	56 (n=101)	60 (n=144)
Prefer not to say	0 (n=0)	1 (n=2)	0.8 (n=2)
Marital status			
Single, never married	57 (n=33)	36 (n=65)	41 (n=98)
Married	40 (n=23)	57 (n=102)	53 (n=125)
Separated	0 (n=0)	3 (n=6)	3 (n=6)
Divorced	3 (n=2)	2 (n=3)	2 (n=5)
Widowed	0 (n=0)	1 (n=2)	0.8 (n=2)
Prefer not to say	0 (n=0)	1 (n=2)	0.8 (n=2)
Education			
Never went to school	0 (n=0)	0 (n=0)	0 (n=0)
Under 16	0 (n=0)	9 (n=17)	7 (n=17)
At 16	2 (n=1)	4 (n=7)	3 (n=8)
Over 16	66 (n=38)	68 (n=122)	67 (n=160)
Not yet finished	33 (n=19)	19 (n=34)	22 (n=53)
Loneliness			
Never	17 (n=10)	12 (n=22)	13 (n=32)
Occasionally	73 (n=42)	69 (n=124)	70 (n=166)
Always	10 (n=6)	19 (n=34)	17 (n=40)

4.2 Defining loneliness

Respondents were asked to describe the feelings of loneliness. Nearly all the participants described loneliness as a negative feeling, regardless of nationality. A few described loneliness as a positive emotion; for example, one respondent said *"I can achieve a spiritual satisfaction when I am lonely"*. Furthermore, a very few described loneliness as a mixed feeling, such as *"When I am lonely, I feel relaxed because I do not need to worry about my social relationships. However, the relaxation does not last long as I start to feel very sad if I am lonely for a very long period"*. Because most respondents described loneliness as an unpleasant feeling, loneliness has been regarded as a negative experience in literature as well, the current chapter focuses on the investigation of loneliness as a negative concept. In total seven themes were identified from the responses. Cultural nuances were also captured. Results are provided below.

4.2.1. Lack of meaningful social connections.

The notion of lack of meaningful social connections is articulated in the way that respondents feel that there is no one they can talk to or to understand them, though they are surrounded by people. This emerged as the most prominent aspect of loneliness in both countries. Typical quotes are:

Extract 1: "*Even though I am surrounded by people and interacting with them, it does not feel like a real connection. Some days when I do not have anything to do I find that I do not have anyone to talk to". (respondent: age 18-24, female, single, UK).*

Extract 2: *"Hoping that someone could understand your situation, offer a listening ear or just being an accompany [sic] without feeling awkward but could not find anyone like this". (respondent: age 25-34, female, single, UK).*

Extract 3: *"I have many friends, but I feel none of them can truly understand me". (respondent: age 25-34, male, married, China).*

Extract 4: *"I have saved a lot of friends' contact information in my phone, but I do not know who I can contact when I want to talk". (respondent: age 25-34, female, single, China).*

4.2.2. Disconnection

Disconnection, i.e. the state of being isolated or detached, is mentioned frequently by respondents from both countries. Based on the source of disconnection, it is further divided into two sub-themes: (1) environmental-related disconnection and (2) perceived disconnection.

The environmental-related disconnection refers to the experienced loneliness as a result of environmental changes, e.g. moving away from home, which is more like a temporary experience than an unchangeable feeling. There is potential for the feeling of loneliness to disappear if individuals can adjust themselves to the new environment or return to the environment they are familiar with. Examples are:

Extract 5: *"I feel lonely when I am in a new place and I do not know anyone well". (respondent: age 18-24, female, single, UK).*

Extract 6: *"I feel lonely because I just moved here [a new place], and this [new] place is far away from city centre". (respondent: age 25-34, female, single, China).*

Extract 7: *"...I would like to go home so that I can be surrounded by my family and friends". (respondent: age 18-24, female, single, China).*

Extract 8: *"Loneliness is an experience of disconnection from friends, family and community. This isolation can occur for many reasons, be that illness, bereavement, being unable to work, or being separated from friends or family by distance and location". (respondent: age 45-54, female, divorced, UK).*

On the other hand, perceived disconnection refers to a sense of detachment from other people or society. Instead of being affected by external factors, it is a reflection of individuals' inner feeling. Example quotes are:

Extract 9: *"Loneliness is a sense of detachment from the world and those I know, even from my parents". (respondent: age 25-34, female, single, UK).*

Extract 10: *"It is the feeling that I am forgotten by the world". (respondent: age 35-44, female, married, China).*

Extract 11: *"I live in a glass bottle; it is so quiet inside but lively outside. However, the outside (of the bottle) has nothing to do with me". (respondent: age 25-34, female, married, China).*

4.2.3. Being alone

Some respondents pointed out that they felt lonely when they were alone or not accompanied by others. Examples include "*I feel lonely when I am alone*", or "*At home alone at [sic] afternoon, I always feel lonely*". Loneliness resulting from being alone may not be necessarily linked to the desire of close relationships; for example, respondents said that *"I feel the need of somebody to be right next to me. Where there is no need to talk, but the physical being is enough"*.

4.2.4. Loss of interests or lack of motivation

Loss of interest or motivation to do anything are typical symptoms of depression (Radloff, 1977). However, they were also used to describe loneliness by respondents from both countries. Chinese respondents tended to have this expression more frequently than British respondents did. Moreover, a few Chinese respondents also associated loneliness with suicidal thoughts. Typical quotes include:

Extract 12: *"I am so sad, boring and I have no interest in anything". (respondent: age 55-64, male, married, China).*

Extract 13: *"I felt I don't have motivation to do anything; the world is meaningless and boring". (respondent: age 25-34, female, separated, China).*

Extract 14: *"I just want to kill myself". (respondent: age 18-24, female, single, China).*

4.2.5. Negative experience

Negative experience can be associated with either past experience or concerns about the future. It covers many different aspects, including (deliberate) social exclusion, being misunderstood, and fear of failure.

Although respondents from both countries have associated negative experience with loneliness, several differences were observed. Firstly, the frequency of linking negative experience with loneliness differed between countries. Compared to respondents from China, respondents from the UK were more likely to mention it; secondly, respondents from the UK tended to associate loneliness with past experience, whereas respondents from China were more likely to link it to the fear of failure in the future. Examples are:

Extract 14: *"…It is particularly when you feel deliberately excluded, not when people are just busy or have other things on their mind". (respondent: age 45-54, female, married, UK).*

Extract 15: *"I feel lonely when I was [sic] not allowed to join in, people cutting me out of activities, sometimes even physically turning their backs on me and cutting off communication. I feel like an alien that is in the wrong place, at the wrong time with no way of changing things". (respondent: age 45-54, male, married, UK).*

Extract 16: *"I feel lonely when people betray me". (respondent: age 45-54, male, married, UK).*

Extract 17: *"I feel lonely when I am isolated, misunderstood". (respondent: age 18-24, male, single, UK).*

Extract 18: *"I worry about failing to achieve my goals". (respondent: age 25-34, female, single, China).*

4.2.6. Lack of support

Lack of support was expressed by respondents from both countries. Examples include *"It [Loneliness] appears when I need help to solve problem. I felt I fight alone against what I like to achieve"*, or *"I have no one rely on, it is as if I am a small ship flowing on the ocean, and it can sink any minute"*. Moreover, the concept of lack of support also includes the fear of lacking support in the future; for example, one respondent said *"…fearing the concept of dying alone, or not being able to have people around me when I most need it"*.

4.2.7. Deficits in social skills

Respondents from both countries also associated social skills with loneliness. This includes lack of proper social skills or loss of confidence in sociability. For example:

Extract 19: *"I want to make friends as other people do, but I just cannot do it properly". (respondent: age 18-24, female, single, China).*

Extract 20: *"I am not confident about my social ability". (respondent: age 25-34, female, single, UK).*

Extract 21: *"Being socially awkward and this not exactly knowing how to make friends; not picking up on all the nuances of social situations". (respondent: age 18-24, female, single, UK).*

Overall, the way loneliness was defined varied between individuals. It is difficult to categorise the descriptions into specific themes as many were related to each other; for example, not having enough support might be associated with lack of meaningful social relationships, and the fear of dying alone could be categorised into negative experience, yet seven common features were captured. In addition, negative emotions were often mentioned associated with feelings of loneliness, such as sadness, emptiness, coldness, hurt, pessimism, unhappiness, etc. Furthermore, some respondents associated loneliness with colours, e.g. grey, black.

4.3 Coping with loneliness

When asking respondents how they cope with loneliness if they have ever felt lonely or they are experiencing loneliness at the moment, distraction emerged as the most prominent theme from both countries. Nearly all respondents said that they distracted themselves from loneliness by doing other tasks, such as watching TV, singing, drawing, writing diaries, exercising, reaching out to friends, etc. Self-distraction may not work well all the time. For example, one respondent said that *"…nothing changes coming home and sitting alone on the sofa in the evening particularly…But finding ways to be connected to others helps, be that through clubs or volunteering in the daytime".*

Another view of coping with loneliness is to accept loneliness. One respondent said that *"I feel happy when I treat loneliness as a friend".* A similar response is *"Treasure it, feel it, taste it and embrace it".* Acceptance also comes with the perception that loneliness is a usual feeling, and no one can get away from it. The specific quote is *"Accept loneliness. Life is a lonely journey; everyone is alone on this journey. If possible, try to make friends and enjoy their company. Friendship can bring joy, but always remember that loneliness is always there regardless of having friends or not. Because people are born alone and die alone".*

Additionally, a few respondents had the belief that time can cure everything including loneliness. On the other hand, unhealthy behaviours were reported, for example, several respondents said that drinking helps to forget loneliness. When asked what strategies work best, most did not give an answer. For those who did, the best strategy was often linked to hobbies or tasks that respondents were interested in. None of the respondents mentioned seeking professional advice to help with overcoming loneliness.

4.4 Reacting to future loneliness – assume one will encounter loneliness at some time in the future

Respondents were asked how they will react to loneliness, assuming that they will experience loneliness at some time in the future. Out of five possible answers (A. *I will actively seek help, e.g. professional advice, re-build social connections*

purposely, go to a place where there are people talking, where I might engage in conversation, such as a café, B. *I will hope that my family or friends will visit me and help me to overcome loneliness instead of asking for their help*, C. *I prefer not to share this, because I do not want others to know that I am lonely*, D. *I don't know* and E. *Other*), over 40% of British respondents and about 52% of Chinese respondents chose answer A, indicating they will adopt a positive strategy to overcome loneliness. The second most frequently chosen answer was B (negatively seeking help) for British respondents and C (unwilling to share loneliness with others) for Chinese respondents (Figure S.3).

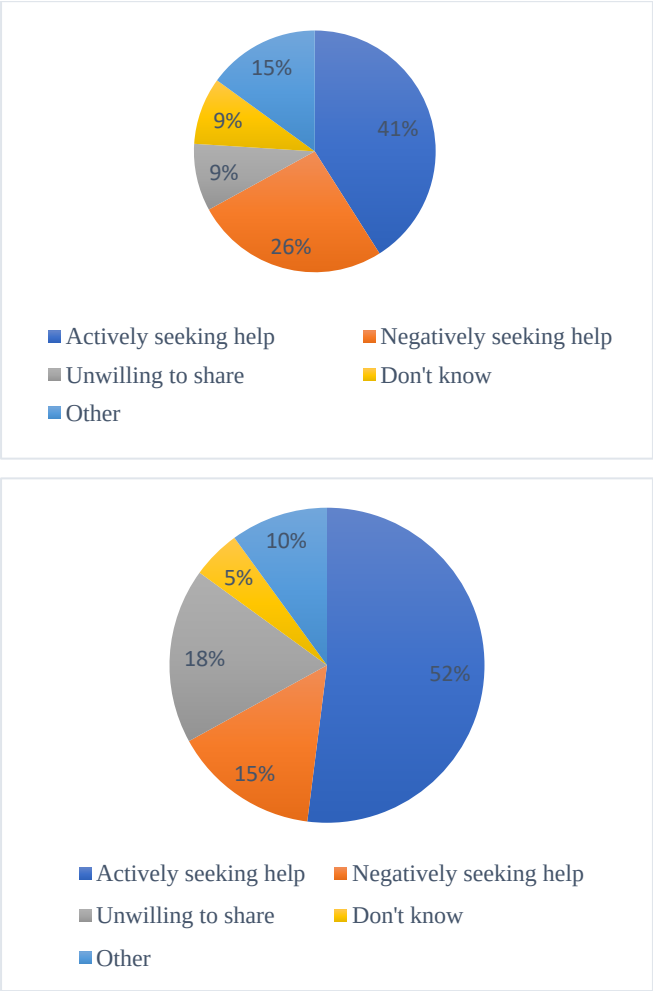


Figure S. 3 Potential coping behaviours mentioned by respondents from the UK and China

Top: Answer from British respondents, Bottom: Answer from Chinese respondents.

Respondents who chose *Other* were further asked to describe how they would overcome loneliness if they were lonely in the future. The common response is to distract themselves from loneliness by doing something they are interested in, which is similar to the coping strategies mentioned earlier. Furthermore, physical health and financial situation were mentioned by British respondents. For example, one respondent said that *"I would actively seek help in the near future but I think it depends on what age you are, it is easier to seek help when you are active and mobile, if you are old, frail and lack mobility becomes much harder to go out and build social connections"*, and another said that *"I don't know about professional help, but would seek out a place to further social connections through education or interests or something – if physically and financially able"*. Apart from that, respondents from both UK and China also reported a combination of positive and negative strategies: they will actively seek help, but also hope that family members and friends would notice their emotional changes and offer help to them.

4.5 Bias against lonely people

When asking whether the society they belong to has any bias against lonely individuals, there was large variation between British and Chinese participants. 43% of British respondents versus 7% of Chinese respondents answered *Yes, there is bias against lonely people*; the percentages of respondents who said *No* were 14% and 48% from UK and China, respectively; and the percentages of respondents who thought bias might exist did not differ substantively between countries (Figure S.4).

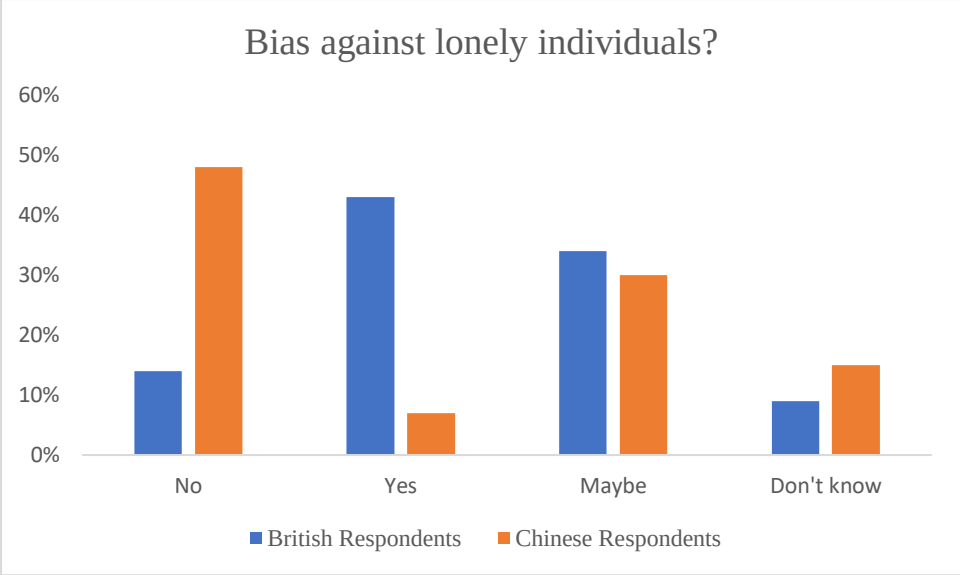


Figure S. 4 Bias against lonely people

Respondents who answered *Yes* were further asked to describe what the bias would be. Three themes were identified: (1) loneliness means emotionally vulnerable, failure, lonely individuals are usually seen as a 'loser', (2) it is their own fault they are lonely because something is wrong with their personality or social skills. Typical quotes supporting this view include *"… people may be blamed for their loneliness or thought of as nasty people if they suffer from it [loneliness] as it is their own fault"*, "*Lonely people are not easy to get along with, they have an exaggerated sense of their own importance"*, or *"Lonely people are responsible for the way they feel"* or *"their loneliness can be alleviated if they made an effort to socialize"*, and (3) lonely people are seen as needy. Examples are *"In the context of ageing I think we are not good at compensating for functional loss (e.g. mobility, sight/hearing) that limits opportunity for social connection, and which creates dependency on others to overcome, reducing a person's own agency"*, *"People may fear lonely people are needy of your time and compassion"*, or *"Lonely people are drama queens, they just want attention from you"*.

Besides the common features, differences were also identified between countries. Respondents from the UK mentioned that society might be responsible for people's loneliness. Examples include *"There are rules that govern how and when people interact. There is a lot of prejudice built around various social hierarchies. Some people do not have permission to speak"*, or *"…huge emphasis put upon extroversion*

and extensive social connections. Not enough emphasis on quality vs quantity". Furthermore, a few British respondents emphasized that the stigma against lonely individuals has something to do with social media as it always exaggerates the importance of having a large social network rather than emphasising the importance of having small but meaningful social connections. This was not mentioned by Chinese respondents.

When asking whether gender difference might exist in terms of getting criticism or bias by admitting loneliness, most respondents from both countries (40% of respondents from UK and 50% of respondents from China) did not think there were differences between men and women. Additionally, 28% and 26% respondents from the UK and China respectively reported that men will encounter more negativity than women (Figure S.5).

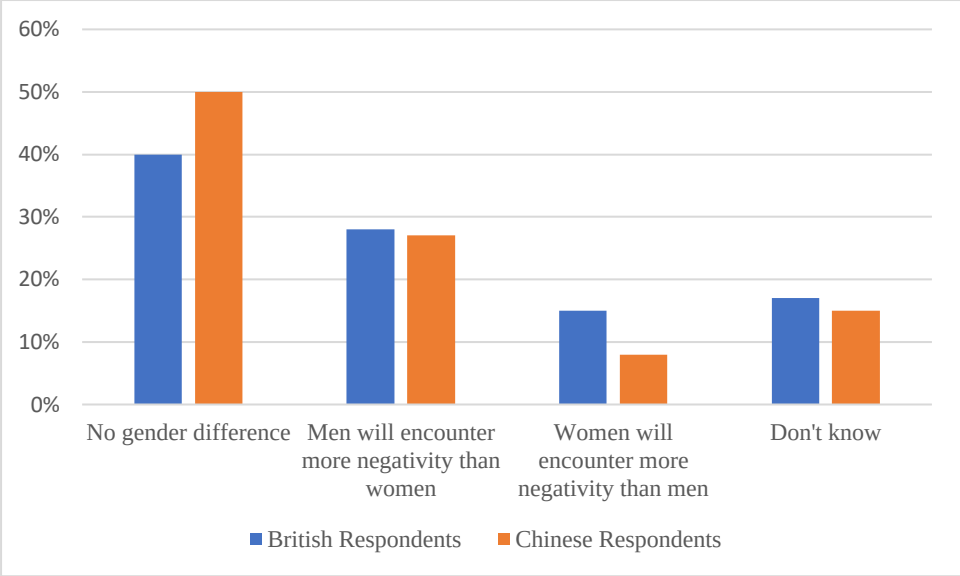


Figure S. 5 Gender difference in terms of encountering criticism or bias by admitting loneliness

4.6 Acceptance of AI as a potential tool to help in preventing and alleviating loneliness

When asking respondents what they think about artificial intelligence and whether it has a role in alleviating loneliness, out of five possible answers (A. *I don't like this idea, and would feel nervous or terrified if artificial intelligence becomes part of my*

daily life; B. *I think a well-developed artificial intelligence can help lonely people as it can be a good companion;* C. *I have no opinion on the subject;* D. *Prefer not to say;* E. *Other*), most respondents (52% of British respondents and 48% of Chinese respondents) showed positive attitudes, but about 12% and 14% claimed that they did not like this idea (Figure S.6).

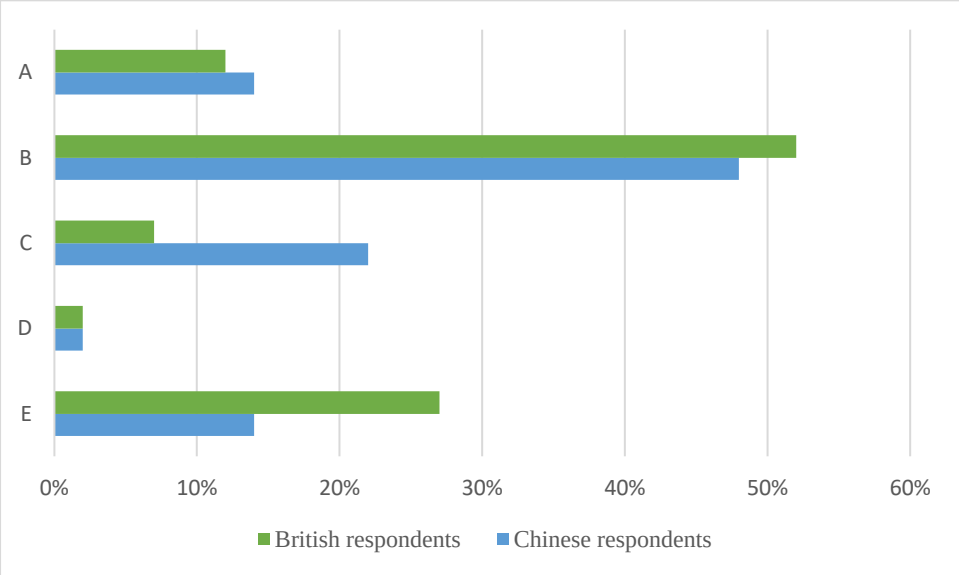


Figure S. 6 The acceptance of AI as a potential tool to help with overcoming loneliness

Note: A: don't like this (AI) idea; B: AI can help with loneliness; C: have no opinion; D: Prefer not to say; E: other.

For respondents who answered *Other*, they were asked to give specific descriptions. Answers from UK and China are largely overlapping with most respondents believing that artificial intelligence cannot fully replace a human being. The answers were further divided into two groups: one indicated that artificial intelligence could help with alleviating loneliness but could not completely eliminate loneliness as AI was not able to provide the true value of social interactions as human beings did; the other group did not think AI would have any impact on loneliness.

Another view is that the effectiveness of artificial intelligence on alleviating loneliness depends on users. Examples include *"I have seen a great potential in AI as a convenient helper in our daily life, but the trick is whether it helps or not depends on users"*, or *"I think it probably depends on the individual person whether it would*

help or not – I can envisage situations where it might help and also at times awareness that it is just an AI robot that might be helping you could in a way make you feel lonelier".

Furthermore, several respondents from both countries expressed concerns that AI would make people feel lonelier. This was because AI was seen to potentially increase the risk of being disconnected from others and diminishes the sense of genuine human interaction. Other concerns towards the use of AI are that it will increase unemployment rate, increase risk of family loss, strengthen social stigma against lonely people or even bring war.

4.7 Acceptance of using AI as a tool to help with loneliness assuming that respondents are suffering from loneliness

In the previous question, respondents were asked whether artificial intelligence would be a useful tool to prevent or alleviate loneliness in general. The current question was aimed at investigating respondents' attitudes towards artificial intelligence use if they were experiencing loneliness. In addition, to further explore the acceptance of artificial intelligence, an answer *"I would like to interact with it even though I am not lonely"* was added. In total, five answers were available for respondents to choose, which were A. *No, I do not like it even though I am lonely and know it may help me (negative);* B. *I would feel comfortable to interact with it and seek its help to alleviate loneliness (positive);* C. *I would like to interact with it even though I am not lonely (very positive);* D. *Prefer not to say;* E. *Other.*

Similarly to the response for the previous question, most respondents (54% from UK and 60% from China) were positive. However, about a quarter of respondents from the UK indicated that they would not use it even though they know it might be helpful. The overall percentage of negative response is higher from China than that from the UK (Figure S.7).

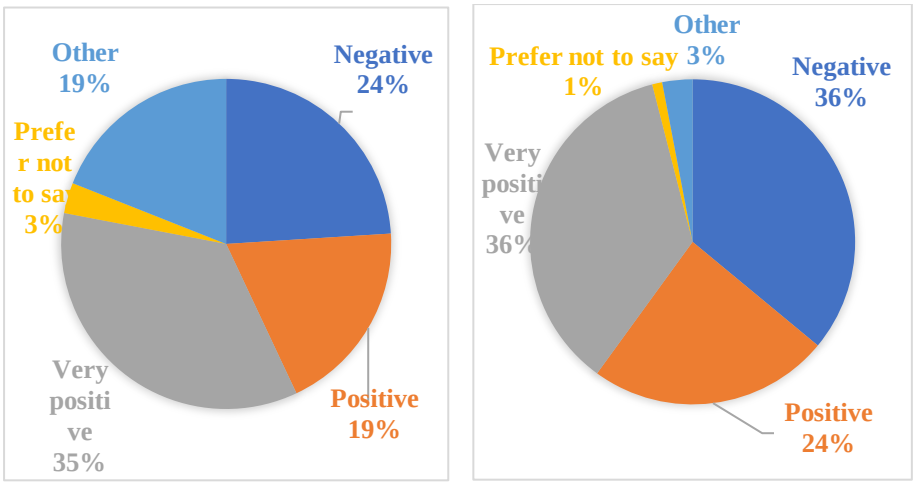


Figure S. 7 The willingness of using AI as an intervention tool to alleviate loneliness if suffering from loneliness

Left: responses from UK; Right: responses from China

When asking respondents to clarify their answer if they chose *Other*, differences appeared between countries. British respondents reported that they prefer animal companions rather than artificial intelligence as a means of alleviating loneliness; a few expressed that they will use artificial intelligence only after there is scientific evidence supporting its effectiveness. Some reported that they will use artificial intelligence on the condition that it is not pretending to be a real human but rather a support, e.g. providing information or suggestions to help lonely individuals deal with loneliness. However, neither animal companions nor the need for evidence were mentioned by Chinese respondents. On the other hand, respondents from China expressed concerns about data confidentiality. One typical quote is *"I will think about it [using artificial intelligence] only when they [the developer, researchers] guarantee they will not leak my personal data".*

4.8 Reaction to the new relaxation of one-child policy: how it will affect the feelings of loneliness

Over half of Chinese respondents believed that the new policy will help with alleviation of loneliness, about a quarter did not think it is going to help, approximately 19% indicated they do not know what its effect will be and an additional 3% had other opinions. The detailed information is shown in Figure S.8.

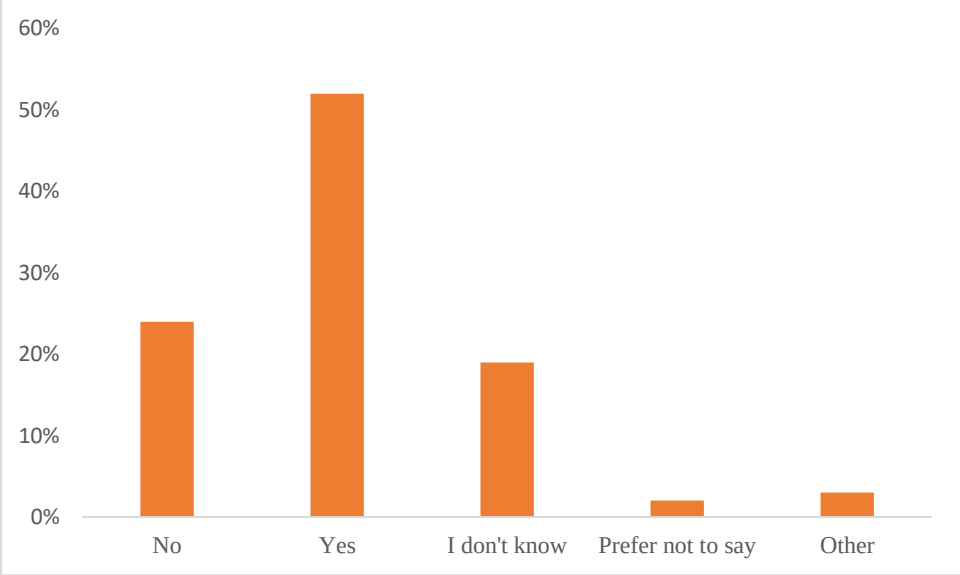


Figure S. 8 Attitudes towards the relaxed one-child policy on potential experience of loneliness

For respondents who had other opinions (chose *Other*), most stated that loneliness was a personal experience that had many causes. Having siblings might be a way to help with loneliness but whether it works or not depends on whether the cause of loneliness is related to lack of companionship.

Respondents who believed the new policy will help with alleviating loneliness stated that having siblings not only means having a companion or confidant with whom they can share their concerns and obtain support, but also it is good for developing better social skills. Most respondents mentioned that they would have better interpersonal relationships if they knew the values of sharing and trusting at a younger age. Some mentioned that having more children could bring more joy to the family.

Individuals who believed the new policy would not help with loneliness said that the new policy may make people feel lonelier, because individuals who were the only child in their family were used to being alone, and having siblings would lower the threshold of feeling lonely. Another view based on a few respondents was that people would be burdened by raising more than one child and also taking care of parents.

5. Discussion

5.1 Summary

This chapter explored how laypeople in two countries, UK and China, conceptualised loneliness. Seven key themes emerged, emphasising meaningful social connection, social disconnection, being alone, loss of interests or motivation, negative experience, social support and social skills. Under the "umbrella" themes, subthemes were also identified. Some themes may be intertwined; for example, negative experience: the fear of dying alone being related to social supports or the lack of close social relationships. Cultural diversities in conceptualisation of loneliness were also captured between countries.

The most frequently used method to handle loneliness was self-distraction, either by doing activities solitarily or interacting with others, i.e. hanging out with friends. Social stigma is believed to exist against loneliness, though whether there are gender differences needs further exploration. Overall, respondents welcome the idea of applying AI in the field of loneliness. Furthermore, positive attitudes towards the new relaxation of the one-child policy were identified. Findings highlighted the subjective nature of loneliness, the need to raise public awareness of loneliness and the areas where interventions can be implemented. An example of potential interventions is shown in Figure S.9.

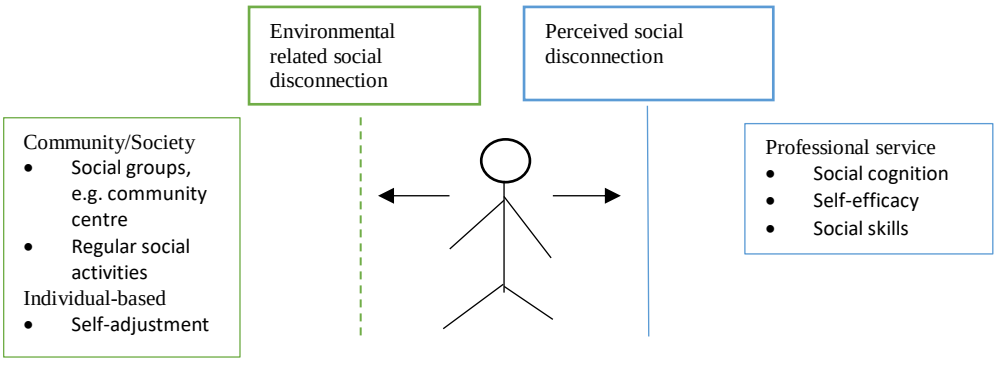


Figure S. 9 An example of intervention drawing upon emerged sub-themes

5.2 Strengths and limitations

Cultural diversity of laypeople's conceptualisation of loneliness has not been investigated in any previous studies; the current study provides evidence to this end. This study did not aim to uncover findings that can be generalised to a larger population, but was intended to provide preliminary evidence on the ways in which loneliness is understood by laypeople. The use of an online platform has many advantages, including access to a large number of respondents regardless of their geographical location, reaching individuals that cannot be reached by other traditional means such as paper-based survey or face-to-face interview. Moreover, it is time-saving and financially cost-effective (Wright, 2005).

The current study has several limitations, notably with regards to its online nature, the small numbers taking part and the limited age range. Although it has many positive attributes for researchers, online studies are subject to sampling issue and non-response bias (Wright, 2005). Social network site users may differ from non-users in their characteristics and preferences; in addition, the use of online social network might be influenced by the offline network and social media features (Hargittai, 2007). Therefore, the heterogeneity between social network site users and non-users could introduce response bias to the findings. The use of snowball sampling may have oversampling issues; individuals who have large social network sizes tend to be oversampled (Heckathorn, 1997). The nature of the researchers' personal social networks may also impact the sampling. This is because individuals who share characteristics, such as age, gender, education level and nationality, with the researchers are more likely to constitute the researchers' social groups.

However, the purpose of the current study was not to capture a representative sample and provide evidence that was generalisable. Instead, it aimed to get a sense of how laypeople in different cultures conceptualise loneliness. Another limitation lies in the bilingual perspective of this study, although survey questions and responses were double-checked by bilingual speakers to ensure consistency. It is possible that the original meanings of some responses were lost during translation and analysis. In addition, as in other cross-national studies, ensuring the optimal equivalence between

the languages and concepts are the biggest challenges. Despite the equivalent term of loneliness existing in Chinese culture, the historical contexts in which the term "loneliness" developed are different between countries. In western cultures, "loneliness" was developed to describe a negative feeling associated with unsatisfying social relationships (Chapter 1, section 1.2.1), whereas in Chinese culture it originally appeared in 《Xunzi》 (i.e. a later compilation of writings associated with Xunzi, a Confucian philosopher; published time: unknown). Loneliness was an adjective term to describe individuals who either lost their parents or their children. The different historical approach to loneliness might play a role in the way people interpret their loneliness; however, in modern society, the term "loneliness" is used to describe the deficits of social relationships in the UK and China.

5.3 Key findings

The understanding of loneliness by laypeople was generally in line with researchers; that is, loneliness is a stressful experience that is related to deficits in social relationships. However, compared to researcher-driven definition, the conceptualisation of loneliness by laypeople had more dimensions. For example, although a few researchers have realised that negative emotions were an aspect of loneliness (de Jong Gierveld, 1998), it was rarely emphasised in studies. However, negative emotions were frequently mentioned by laypeople when describing their feelings of loneliness. Moreover, from a lay perspective, the deficits in personality and social skills might be a source of loneliness; again, these were not captured by researchers. Furthermore, despite both researchers and laypeople noting that loneliness was associated with personal experience, researchers emphasised that loneliness itself was a personal experience which varied between individuals; whereas, laypeople put an emphasis on the association between loneliness and negative events, either past events or the fear of future negative events.

Additionally, different thresholds of loneliness were identified. For most people, loneliness was related to lack of meaningful social connections with others, placing an emphasis on the qualitative aspect of social relationships; whereas, for some respondents, simply not being surrounded by people or being alone was associated with loneliness. Cultural differences were also observed, of which the most striking

was that, compared to British respondents, Chinese respondents were more likely to interpret loneliness and depression interchangeably. Table S.3 summarises the conceptualisation of loneliness and comparisons between the two countries.

Regarding coping strategies, self-distraction was identified as the most frequently used strategy by respondents. For most respondents, self-distraction was implemented by directing attention to hobbies or unharmful tasks, such as listening to music, exercising, doing housework; whereas, for some others, self-distraction was instigated through unhealthy behaviours, such as drinking. Notably none of the respondents from either country has mentioned seeking help from professionals. Without any further descriptions, it is difficult to know whether this was due to limited availability of professional resources, or respondents did not know of the existence of professional help (e.g. psychological supporting service such as cognitive behaviour therapy group and counselling services run by local authorities), or both. Moreover, it might be that previous experiences of criticism deter lonely individuals from seeking help from professionals. In Chapter 7, loneliness was found to be associated with increased health service and social care usage. However, none of those services was designed specifically to help alleviate loneliness. Therefore, the easily-accessible professional services that particularly target loneliness not only help with alleviating loneliness, but also have a great potential to reduce unnecessary health-related costs.

In terms of bias, respondents from both countries stated that there was bias against lonely individuals in their society, though this was reported by a much larger percentage of British respondents than those in China. Lonely people were seen as a "loser", needy, having personality issues and bad social skills, suggesting that the public thinks it is lonely individuals' own fault that they are lonely. This finding is supported by findings from another qualitative study based on older Norwegians, in which researchers found that the dominant explanation of individuals' loneliness was that it was lonely individuals' own fault and was due to their way of behaving (Hauge and Kirkevold, 2010). The finding from the current study also provided insights into different cultural perspectives. British respondents specifically mentioned that the criticisms against lonely individuals were related to society's strict hierarchy and social media's exaggeration of social relationships, which was that instead of placing the importance on having meaningful relationships, social media emphasised that

having large social networks is a status of success. This finding is important as it provides evidence and potential means for policy makers and social media to eliminate social stigma towards lonely people.

With regard to the acceptance of AI as a potential intervention tool for preventing or alleviating loneliness, the finding is optimistic, with most respondents saying that they would like to interact with AI, but with very important reservations that need attention. Also of note is that nearly all respondents were aged between 18 to 54 years. Further research targeting older age is very much required.

Similar to the acceptance of AI, the finding on laypeople's (Chinese respondents') attitudes towards relaxation of the one-child policy is optimistic. Over half believed it would help with avoidance of feeling lonely. Although most respondents recognised that loneliness is a personal feeling that may have little to do with the number of family members, they believed that having siblings means having close companions, support, and is good for developing interpersonal skills, and the social skills developed in childhood will help people to have better social relationships in adulthood.

Table S. 3 Summary of responses by country

	British Respondents	Chinese Respondents
Defining loneliness (seven themes)		
Lack of meaningful social connection	***	***
Disconnection		
• Environmental-related	**	**
• Perceived	**	**
Being alone	*	*
Loss of interests or motivation	*	**
Negative experience		
• Past experience	**	*
• Fear for future	*	**
Lack of support	*	*
Deficits in social skills	*	*
Coping loneliness		
Self-distraction	***	***
Accept loneliness	*	*
Do nothing or negative behaviours	*	*
Criticism and bias against lonely people		
Vulnerability, failure	***	***
Personality issue or deficits in social skills	**	**
Needy	**	**
Social hierarchy / exaggeration on social relationships	**	-
Gender differences in terms of bias		
No	***	***
AI as a potential intervention tool		
High acceptance	***	***
Attitudes towards relaxed one-child policy		
Positive	NA	***

Note: larger number of * indicates a higher percentage of responses; "-": no response; NA: not applicable.

The experience of loneliness can change over time (Chapter 4); the current study highlighted areas that can be modified to help with alleviation of loneliness, notably with regards to developing threshold-specific and cause-specific prevention programmes. Moreover, in order to reduce social stigma, policy makers and researchers need to raise public awareness of loneliness, place an emphasis on its

multi-dimensional causes so people can learn more about the complexity of loneliness, and be less critical towards lonely individuals; in addition, professional services should be made more readily available.

6. Conclusion

This chapter explored how individuals conceptualise loneliness, what strategies they use to cope with loneliness, the bias and criticism towards lonely individuals, as well as the acceptability of artificial intelligence as a potential tool to prevent or alleviate loneliness. The findings highlight lack of meaningful social connections as the most prominent theme amongst constructs of loneliness. The results also reveal individual differences in terms of triggers and thresholds of loneliness. With regard to coping strategies, self-distraction is found to be the most frequently used method to overcome loneliness. To this end, the results highlight the importance of developing professional services and the need to make it publicly accessible. Bias against lonely individuals exists, with a slightly higher proportion of respondents believing men would encounter more negativity than women; public officials need to develop strategies to reduce social stigma. Artificial intelligence is highly acceptable, implying a great potential for implementing AI in the field of loneliness in the future. Although findings have fundamental underpinning shared by countries, cultural diversities exist.

Despite the methodological limitations on the generalisation of the findings, the study highlights the unique ways in which loneliness is understood in different cultures. In addition, the distribution of characteristics of respondents was similar between countries, which makes the direct comparison more suitable. The study of loneliness is burgeoning, but the evidence on how the public perceives loneliness is still limited; moreover, evidence on the cultural perspective of loneliness is scant. The current study takes the first step towards capturing loneliness in which it has culturally diverse perspectives. Further investigation including multiple countries and different age groups is required.

Appendix S.1 Information sheet of cross-cultural perspectives of loneliness

UNIVERSITY OF CAMBRIDGE

Institute of Public Health
Forvie Site, Robinson Way
Cambridge CB2 0SR
Telephone 01223 330300

Cross-cultural perspective on loneliness

Dear participants,

Thank you very much for opening this page about a study from the University of Cambridge about loneliness in the UK and China. The purpose of this study is to learn more about how people define and experience loneliness, along with what we do to combat loneliness when we feel it.

It is anonymous, you do not need to give your name and cannot be identified. However, you have to be 18 years or older to answer it. The survey questions take about ten minutes to complete. There are no benefits for you in answering these, but your responses will help understand loneliness better, and, we hope, contribute to the ways that we can tackle loneliness in the future.

At each stage, you have to answer the question to continue to the next one. However, you can choose "prefer not to say" for questions that concern you or make you uncomfortable. When research results are published, individual responses cannot be identified.

We would be really appreciated if you can pass the link for the study on to others who you know might be interested in helping us.

This research is part of my PhD study, and it is not founded by any organizations. If you have any questions regarding of this study, please do not hesitate to contact me at hw448@medschl.cam.ac.uk.

Thank you for your time.

Sincerely,
Hanyuying Wang

Appendix S.2 Questionnaire of cross-cultural perspectives of loneliness

1. Age in years *

- [ ] Under 18, not eligible for this study, please do not proceed to further questions
- [ ] 18-24
- [ ] 25-34
- [ ] 35-54
- [ ] 55-64
- [ ] 65-74
- [ ] 75+
- [ ] Prefer not to say

2. Gender *

- [ ] Male
- [ ] Female
- [ ] Prefer not to say

3. Marital status *

- ( ) Single, Never Married
- ( ) Married
- ( ) Separated
- ( ) Divorced
- ( ) Widowed
- ( ) Prefer not to say

4. At what age did you finish your full-time education at school? *

5. Do you feel lonely? *

- ○ Never
- ○ Yes, occasionally
- ○ Yes, always
- ○ Prefer not to say

6. What is your experience of loneliness? Please use few sentences to describe how you would describe the feeling. Please fill NA if not applicable or you prefer not to say.
*

7. If you have ever felt lonely or are experiencing loneliness at the moment, how do you cope with these feelings? What do you find works best for you? If you have never felt lonely, please skip this question and go to next question. Please fill NA if not applicable or you prefer not to say.

8. Do you think loneliness is to be expected as we age?
*

- ○ No
- ○ Probably not
- ○ Probably is
- ○ Yes
- ○ Prefer not to say

9. Assuming that you have feelings of loneliness at some time in the future, how do you think you might react to this?
*

- ○ I will actively seek help (e.g. professional advice, re-build social connections purposely, go to a place where there are people talking, where I might engage in conversations, such as a café)
- ○ I will hope that my family or friends will visit me and help me to overcome loneliness instead of asking for their help
- ○ I prefer not to share this, because I do not want others to know that I am lonely
- ○ I don't know
- ○ Other (please specify):

10. Do you think the society you belong to has any bias against lonely people? *

- ○ No
- ○ Yes
- ○ Maybe
- ○ I don't know
- ○ Prefer not to say

If you have answered Yes, please explain what bias that might be

11. Do you think men might encounter more criticism or bias by admitting their loneliness than women? Or could it be the other way around? *

- ○ I think there would be no differences between men and women
- ○ Yes, men will encounter more negativity than women
- ○ No, women will encounter more negativity than men
- ○ I don't know
- ○ Prefer not to say

12. This survey is anonymous, but if we had asked these questions in a setting where it is not an anonymous, would you have wanted to answer the questions? *

- ○ No
- ○ Yes
- ○ Not sure

13. Artificial intelligence (A.I.) has seeped its way into our lives, such as a smart phone installed assistant like Siri, robot surgeons, etc. In addition, the design of auto-driving vehicles is underway. The development of A.I. is moving from algorithm-based to neural-network-based, which means that A.I. will be free of pre-defined functions and have self-learning ability or even personal feelings. The benefits (or harm) it will bring to our lives may be beyond our imagination. What do you think about A.I.? Do you think A.I. will have a role in alleviating loneliness?

*

- ○ I do not like this idea, and would feel nervous or terrified if A.I. becomes part of my daily life
- ○ I think a well-developed A.I. can help lonely people as it can be a good companion
- ○ I have no opinion on the subject
- ○ Prefer not to say
- ○ Other (please specify):

14. If you are suffering loneliness and an A.I. robot was available to you, would you use it to help overcome your feelings of distress?

*

- ○ No, I do not like it even though I am lonely and know it may help me
- ○ I would feel comfortable to interact with it and seek its help to alleviate loneliness
- ○ I would like to interact with it even though I am not lonely
- ○ Prefer not to say
- ○ Other (please specify):

15. For Chinese participants only

Since November 2013, the government has relaxed the one-child policy, do you think this new policy will have any impact on your answer regarding the future? *

- ○ No
- ○ Yes
- ○ I don't know
- ○ Prefer not to say
- ○ Other (please specify):

If you have answered No/Yes, please explain your reasons why you think so

References

Adams, G., Anderson, S. L., & Adonu, J. K. (2004). The cultural grounding of closeness and intimacy. *Handbook of closeness and intimacy*, 324-325.

Aguirre-Hernández, R., & Farewell, V. (2002). A Pearson-type goodness-of-fit test for stationary and time-continuous Markov regression models. *Statistics in Medicine, 21*(13), 1899-1911.

Amieva, H., Jacqmin-Gadda, H., Orgogozo, J.-M., Le Carret, N., Helmer, C., Letenneur, L., . . . Dartigues, J.-F. (2005). The 9 year cognitive decline before dementia of the Alzheimer type: a prospective population-based study. *Brain, 128*(5), 1093-1101.

Andren, K. G., & Rosenqvist, U. (1985). Heavy users of an emergency department: psycho-social and medical characteristics, other health care contacts and the effect of a hospital social worker intervention. *Soc Sci Med, 21*(7), 761-770.

Andren, K. G., & Rosenqvist, U. (1987). Heavy users of an emergency department--A two year follow-up study. *Social science & medicine, 25*(7), 825-831.

Antonucci, T. C., & Israel, B. A. (1986). Veridicality of social support: A comparison of principal and network members' responses. *Journal of Consulting and Clinical Psychology, 54*(4), 432.

Association, A. P. (1980). *Tardive dyskinesia*: American Psychiatric Association.

Austin, P. C., & Stuart, E. A. (2015). Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Statistics in medicine*, 34(28), 3661-3679.

Azur, M. J., Stuart, E. A., Frangakis, C., & Leaf, P. J. (2011). Multiple imputation by chained equations: what is it and how does it work? *International journal of methods in psychiatric research, 20*(1), 40-49.

Banks, M. R., Willoughby, L. M., & Banks, W. A. (2008). Animal-assisted therapy and loneliness in nursing homes: use of robotic versus living dogs. *Journal of the American Medical Directors Association, 9*(3), 173-177.

Barnes, L. L., Mendes de Leon, C. F., Wilson, R. S., Bienias, J. L., & Evans, D. A. (2004). Social resources and cognitive decline in a population of older African Americans and whites. *Neurology, 63*(12), 2322.

Berg, S., Mellström, D., Persson, G., & Svanborg, A. (1981). Loneliness in the Swedish aged. *Journal of Gerontology, 36*(3), 342-349.

Berkman, L. F. (1985). The relationship of social networks and social support to morbidity and mortality.

Berkman, L. F., & Syme, S. L. (1979). Social networks, host resistance, and mortality: a nine-year follow-up study of Alameda County residents. *American Journal of Epidemiology, 109*(2), 186-204.

Berkman, L., & Karachi, I. (2000). Social Epidemiology. *Oxford: Oxford University Press.*

Beutel, M. E., Klein, E. M., Brähler, E., Reiner, I., Jünger, C., Michal, M., . . . Tibubos, A. N. (2017). Loneliness in the general population: Prevalence, determinants and relations to mental health. *BMC Psychiatry, 17*.

Bickerdike, L., Booth, A., Wilson, P. M., Farley, K., & Wright, K. (2017). Social prescribing: less rhetoric and more reality. A systematic review of the evidence. *BMJ Open, 7*(4), e013384.

Biernacki, P., & Waldorf, D. (1981). Snowball sampling: Problems and techniques of chain referral sampling. *Sociological methods & research, 10*(2), 141-163.

Bock, J. O., Hajek, A., & König, H. H. (2017). The longitudinal association between psychological factors and health care use. *Health services research*.

Borys, S., & Perlman, D. (1985). Gender differences in loneliness. *Personality and Social Psychology Bulletin, 11*(1), 63-74.

Boss, L., Kang, D.-H., & Branson, S. (2015). Loneliness and cognitive function in the older adult: a systematic review. *International Psychogeriatrics, 27*(4), 541-553.

Bowlby, J. (1969). *Attachment and Loss: Attachment.-1969.-(RUidnr.: M102591232)*: Basic books.

Braun, V., & Clarke, V. (2006). Using thematic analysis in psychology. *Qualitative research in psychology, 3*(2), 77-101.

Brayne, C., Matthews, F. E., McGee, M. A., & Jagger, C. (2001). Health and ill-health in the older population in England and Wales. The Medical Research Council Cognitive Function and Ageing Study (MRC CFAS). *Age Ageing, 30*(1), 53-62.

Brayne, C., Spiegelhalter, D. J., Dufouil, C., Chi, L. Y., Dening, T. R., Paykel, E. S., . . . Huppert, F. A. (1999). Estimating the true extent of cognitive decline in the old old. *Journal of the American Geriatrics Society, 47*(11), 1283-1288.

Brittain, K., Kingston, A., Davies, K., Collerton, J., Robinson, L. A., Kirkwood, T. B., . . . Jagger, C. (2017). An investigation into the patterns of loneliness and loss in the oldest old–Newcastle 85+ study. *Ageing & Society, 37*(1), 39-62.

Broekens, J., Heerink, M., & Rosendal, H. (2009). Assistive social robots in elderly care: a review. *Gerontechnology, 8*(2), 94-103.

Burr, J. A., & Lee, H. J. (2013). Social relationships and dental care service utilization among older adults. *Journal of aging and health, 25*(2), 191-220.

Birbili, M. (2000). Translating from one language to another. *Social research update, 31*(1), 1-7.

Cacioppo, J. T., & Cacioppo, S. (2014). Social relationships and health: The toxic effects of perceived social isolation. *Social and personality psychology compass,* 8(2), 58-72.

Cacioppo, J. T., Hawkley, L. C., Berntson, G. G., Ernst, J. M., Gibbs, A. C., Stickgold, R., & Hobson, J. A. (2002). Do lonely days invade the nights? Potential social modulation of sleep efficiency. *Psychological Science, 13*(4), 384-387.

Cacioppo, J. T., Hawkley, L. C., & Thisted, R. A. (2010). Perceived social isolation makes me sad: 5-year cross-lagged analyses of loneliness and depressive symptomatology in the Chicago Health, Aging, and Social Relations Study. *Psychology and aging, 25*(2), 453.

Caspi, A., Harrington, H., Moffitt, T. E., Milne, B. J., & Poulton, R. (2006). Socially isolated children 20 years later: risk of cardiovascular disease. *Archives of Pediatrics & Adolescent Medicine, 160*(8), 805-811.

Cassel, J. (1976). The contribution of the social environment to host resistance: the Fourth Wade Hampton Frost Lecture. *American Journal of Epidemiology, 104*(2), 107-123.

Cattan, M., White, M., Bond, J., & Learmouth, A. (2005). Preventing social isolation and loneliness among older people: a systematic review of health promotion interventions. *Ageing & Society, 25*(1), 41-67.

Charles, D., Paul, E., & Phillip, P. (1872). The expression of the emotions in man and animals. *Electronic Text Center, University of Virginia Library*.

Charles, S., & Carstensen, L. L. (2010). Social and Emotional Aging. *Annual Review of Psychology, 61*, 383-409. doi:10.1146/annurev.psych.093008.100448

Chen, H. Y., & Boore, J. R. (2010). Translation and back-translation in qualitative nursing research: methodological review. *Journal of clinical nursing, 19*(1-2), 234-239.

Cheng, S. T. (1992). Loneliness-distress and physician utilization in well-elderly females. *Journal of Community Psychology, 20*(1), 43-56.

Chou, K. L., & Chi, I. (2002). Successful aging among the young-old, old-old, and oldest-old Chinese. *Int J Aging Hum Dev, 54*(1), 1-14. doi:10.2190/9k7t-6kxm-c0c6-3d64

Cobb, S. (1979). Social support and health through the life course In MW Riley (Ed,), Aging from birth to death: Interdisciplinary perspectives (pp. 93-106). *Boulder, CO1 Westview*.

Cohen, S. (1988). Psychosocial models of the role of social support in the etiology of physical disease. *Health psychology, 7*(3), 269.

Cohen, S., & Wills, T. A. (1985). Stress, social support, and the buffering hypothesis. *Psychological Bulletin, 98*(2), 310.

Cohen-Mansfield, J., & Parpura-Gill, A. (2007). Loneliness in older persons: a theoretical model and empirical findings. *International Psychogeriatrics, 19*(2), 279-294.

Cooper, C. (2013). Loneliness is the reason one in 10 visit their GP claims charity. Retrieved from https://www.independent.co.uk/life-style/health-and-families/health-news/charity-claims-loneliness-is-the-reason-one-in-10-visit-their-gp-8940392.html

Cox, D. R. (1972). Regression Models and Life-Tables. *Journal of the Royal Statistical Society. Series B (Methodological), 34*(2), 187-220.

Coyle, C. E., & Dugan, E. (2012). Social isolation, loneliness and health among older adults. *Journal of aging and health, 24*(8), 1346-1363.

Cutrona, C., & Russell, D. (1983). *The Provisions of Social Relationships and Adaptation to Stress* (Vol. 1).

Dahlberg, L., Andersson, L., McKee, K. J., & Lennartsson, C. (2015). Predictors of loneliness among older women and men in Sweden: A national longitudinal study. *Aging & mental health, 19*(5), 409-417.

Davies, K., Collerton, J. C., Jagger, C., Bond, J., Barker, S. A. H., Edwards, J., . . . Robinson, L. (2010). Engaging the oldest old in research: lessons from the Newcastle 85+ study. *BMC Geriatr, 10*, 64. doi:10.1186/1471-2318-10-64

de Jong Gierveld, J. (1998). A review of loneliness: concept and definitions, determinants and consequences. *Reviews in Clinical Gerontology, 8*(1), 73-80.

de Jong Gierveld, J., & Van Tilburg, T. (1999). Manual of the Loneliness Scale. *Onbekend*.

de Jong Gierveld, J., & Van Tilburg, T. (2006). A 6-item scale for overall, emotional, and social loneliness: Confirmatory tests on survey data. *Research on Aging, 28*(5), 582-598.

de Jong Gierveld, J., Van der Pas, S., & Keating, N. (2015). Loneliness of older immigrant groups in Canada: Effects of ethnic-cultural background. *Journal of Cross-Cultural Gerontology, 30*(3), 251-268.

De Silva, A. P., Moreno-Betancur, M., De Livera, A. M., Lee, K. J., & Simpson, J. A. (2017). A comparison of multiple imputation methods for handling missing values in longitudinal data in the presence of a time-varying covariate with a non-linear association with time: a simulation study. *BMC Medical Research Methodology, 17*(1), 114.

Dickens, A. P., Richards, S. H., Hawton, A., Taylor, R. S., Greaves, C. J., Green, C., . . . Campbell, J. L. (2011). An evaluation of the effectiveness of a community mentoring service for socially isolated older people: a controlled trial. *BMC Public Health, 11*(1), 218. doi:10.1186/1471-2458-11-218

Diggle, P., Diggle, P. J., Heagerty, P., Heagerty, P. J., Liang, K.-Y., & Zeger, S. (2002). *Analysis of longitudinal data*: Oxford University Press.

DiNapoli, E. A., Wu, B., & Scogin, F. (2014). Social isolation and cognitive function in Appalachian older adults. *Research on Aging, 36*(2), 161-179.

DiTommaso, E., Brannen-McNulty, C., Ross, L., & Burgess, M. (2003). Attachment styles, social skills and loneliness in young adults. *Personality and Individual Differences, 35*(2), 303-312.

DiMatteo, M. R. (2004). Social support and patient adherence to medical treatment: a meta-analysis. Health psychology, 23(2), 207.

Drageset, J., Kirkevold, M., & Espehaug, B. (2011). Loneliness and social support among nursing home residents without cognitive impairment: A questionnaire

survey. *International Journal of Nursing Studies, 48*(5), 611-619. doi:https://doi.org/10.1016/j.ijnurstu.2010.09.008

Dufouil, C., Clayton, D., Brayne, C., Chi, L., Dening, T., Paykel, E., . . . Huppert, F. (2000). Population norms for the MMSE in the very old estimates based on longitudinal data. *Neurology, 55*(11), 1609-1613.

Dugan, E., & Kivett, V. R. (1994). The importance of emotional and social isolation to loneliness among very old rural adults. *The Gerontologist, 34*(3), 340-346.

Durkheim, E. (1951). Suicide: a study in sociology [1897]. *Translated by JA Spaulding and G. Simpson (Glencoe, Illinois: The Free Press, 1951)*.

Dyal, S. R., & Valente, T. W. (2015). A systematic review of loneliness and smoking: Small effects, big implications. *Substance use & misuse, 50*(13), 1697-1716.

Dykstra, P. A. (2009). Older adult loneliness: myths and realities. *European journal of ageing, 6*(2), 91.

Dykstra, P. A., & de Jong Gierveld, J. (2004). Gender and marital-history differences in emotional and social loneliness among Dutch older adults. *Canadian Journal on Aging/la revue canadienne du vieillissement, 23*(2), 141-155.

Dykstra, P. A., Van Tilburg, T. G., & Gierveld, J. d. J. (2005). Changes in older adult loneliness: Results from a seven-year longitudinal study. *Research on Aging, 27*(6), 725-747.

Ejlskov, L., Wulff, J., Boggild, H., Kuh, D., & Stafford, M. (2017). Assessing the relative importance of correlates of loneliness in later life. Gaining insight using recursive partitioning. *Aging Ment Health*, 1-8. doi:10.1080/13607863.2017.1370690

Ellaway, A., Wood, S., & Macintyre, S. (1999). Someone to talk to? The role of loneliness as a factor in the frequency of GP consultations. *Br J Gen Pract, 49*(442), 363-367.

Ellwardt, L., van Tilburg, T., Aartsen, M., Wittek, R., & Steverink, N. (2015). Personal networks and mortality risk in older adults: a twenty-year longitudinal study. *PloS one, 10*(3), e0116731.

Fees, B. S., Martin, P., & Poon, L. W. (1999). A model of loneliness in older adults. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 54*(4), P231-P239.

Fischer, C. S. (1982). To dwell among friends: Personal networks in town and city. University of chicago Press.

Fleming, J., Zhao, E., O'connor, D. W., Pollitt, P. A., Brayne, C., & Farquhar, M. (2007). Cohort profile: the Cambridge City over-75s Cohort (CC75C). *International journal of epidemiology*, *36*(1), 40-46.

Fokkema, T., & Knipscheer, K. (2007). Escape loneliness by going digital: A quantitative and qualitative evaluation of a Dutch experiment in using ECT to overcome loneliness among older adults. In: Taylor & Francis.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). "Mini-mental state". A practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res*, *12*(3), 189-198.

Geller, J. (2004). Loneliness and pregnancy in an urban Latino community: Associations with maternal age and unscheduled hospital utilization. *Journal of Psychosomatic Obstetrics & Gynecology*, *25*(3-4), 203-209.

Geller, J., Janson, P., McGovern, E., & Valdini, A. (1999). Loneliness as a predictor of hospital emergency department use. *J Fam Pract*, *48*(10), 801-804.

Gentleman, R., Lawless, J., Lindsey, J., & Yan, P. (1994). Multi-state Markov models for analysing incomplete disease history data with illustrations for HIV disease. *Statistics in Medicine*, *13*(8), 805-821.

Gerst-Emerson, K., & Jayawardhana, J. (2015). Loneliness as a Public Health Issue: The Impact of Loneliness on Health Care Utilization Among Older Adults. *American Journal of Public Health*, *105*(5), 1013-1019. doi:10.2105/AJPH.2014.302427

Girling, D. M., Huppert, F. A., Brayne, C., Paykel, E. S., Gill, C., & Mathewson, D. (1995). Depressive symptoms in the very elderly—their prevalence and significance. International Journal of Geriatric Psychiatry, 10(6), 497-504.

Gomes, B., & Higginson, I. J. (2006). Factors influencing death at home in terminally ill patients with cancer: systematic review. *Bmj*, *332*(7540), 515-521.

Gottlieb, B. H., Cohen, S., Underwood, L. G., & Gottlieb, B. (2000). Social support measurement and intervention: A guide for health and social scientists. In: New York, Oxford University Press, Inc.

Gow, A. J., Corley, J., Starr, J. M., & Deary, I. J. (2013). Which social network or support factors are associated with cognitive abilities in old age? *Gerontology*, *59*(5), 454-463.

Graham, J. W., Olchowski, A. E., & Gilreath, T. D. (2007). How many imputations are really needed? Some practical clarifications of multiple imputation theory. *Prevention science, 8*(3), 206-213.

Green, L. R., Richardson, D. S., Lago, T., & Schatten-Jones, E. C. (2001). Network correlates of social and emotional loneliness in young and older adults. *Personality and Social Psychology Bulletin, 27*(3), 281-288.

Haines, N. (2017). Divorces in England and Wales: 2016. Statistical bulletin.

Hand, C., McColl, M. A., Birtwhistle, R., Kotecha, J. A., Batchelor, D., & Barber, K. H. (2014). Social isolation in older adults who are frequent users of primary care services. *Can Fam Physician, 60*(6), e322, e324-329.

Hardt, J., Herke, M., & Leonhart, R. (2012). Auxiliary variables in multiple imputation in regression with missing X: a warning against including too many in small sample research. *BMC Medical Research Methodology, 12*(1), 184. doi:10.1186/1471-2288-12-184

Hargittai, E. (2007). Whose space? Differences among users and non-users of social network sites. *Journal of Computer-Mediated Communication, 13*(1), 276-297.

Harris, R. A., Qualter, P., & Robinson, S. J. (2013). Loneliness trajectories from middle childhood to pre-adolescence: impact on perceived health and sleep disturbance. *Journal of Adolescence, 36*(6), 1295-1304.

Hauge, S., & Kirkevold, M. (2010). Older Norwegians' understanding of loneliness. *International Journal of Qualitative Studies on Health and Well-being, 5*(1), 4654.

Havens, B., Hall, M., Sylvestre, G., & Jivan, T. (2004). Social Isolation and Loneliness: Differences between Older Rural and Urban Manitobans. *Canadian Journal on Aging / La Revue canadienne du vieillissement, 23*(2), 129-140. doi:10.1353/cja.2004.0022

Hawker, M., & Romero-Ortuno, R. (2016). Social Determinants of Discharge Outcomes in Older People Admitted to a Geriatric Medicine Ward. *J Frailty Aging, 5*(2), 118-120. doi:10.14283/jfa.2016.89

Hawkley, L. C., & Cacioppo, J. T. (2010). Loneliness matters: a theoretical and empirical review of consequences and mechanisms. *Annals of behavioral medicine, 40*(2), 218-227.

Hawkley, L. C., Hughes, M. E., Waite, L. J., Masi, C. M., Thisted, R. A., & Cacioppo, J. T. (2008). From social structural factors to perceptions of relationship quality and loneliness: the Chicago health, aging, and social relations study. *The Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 63*(6), S375-S384.

Hawkley, L. C., & Kocherginsky, M. (2017). Transitions in Loneliness Among Older Adults: A 5-Year Follow-Up in the National Social Life, Health, and Aging Project. *Research on Aging, 40*(4), 365-387. doi:10.1177/0164027517698965

Hawkley, L. C., Thisted, R. A., & Cacioppo, J. T. (2009). Loneliness predicts reduced physical activity: cross-sectional & longitudinal analyses. *Health psychology, 28*(3), 354.

Hawkley, L. C., Thisted, R. A., Masi, C. M., & Cacioppo, J. T. (2010). Loneliness predicts increased blood pressure: 5-year cross-lagged analyses in middle-aged and older adults. *Psychology and aging, 25*(1), 132.

Heckathorn, D. D. (1997). Respondent-driven sampling: a new approach to the study of hidden populations. *Social problems, 44*(2), 174-199.

Heylen, L. (2010). The older, the lonelier? Risk factors for social loneliness in old age. *Ageing & Society, 30*(7), 1177-1196.

Hernan, M., & Robins, J. (2017). Causal Inference. *Boca Raton: Chapman & Hall/CRC*.

Holmén, K., Ericsson, K., & Winblad, B. (2000). Social and emotional loneliness among non-demented and demented elderly people. *Archives of Gerontology and Geriatrics, 31*(3), 177-192.

Holmén, K., & Furukawa, H. (2002). Loneliness, health and social network among elderly people—a follow-up study. *Archives of Gerontology and Geriatrics, 35*(3), 261-274.

Holt-Lunstad, J., Smith, T. B., Baker, M., Harris, T., & Stephenson, D. (2015). Loneliness and social isolation as risk factors for mortality: a meta-analytic review. *Perspectives on Psychological Science, 10*(2), 227-237.

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: a meta-analytic review. *PLoS medicine, 7*(7), e1000316.

Holwerda, T. J., Deeg, D. J., Beekman, A. T., van Tilburg, T. G., Stek, M. L., Jonker, C., & Schoevers, R. A. (2012). Feelings of loneliness, but not social isolation,

predict dementia onset: results from the Amsterdam Study of the Elderly (AMSTEL). *J Neurol Neurosurg Psychiatry*, jnnp-2012-302755.

House, J. S. (1983). Work stress and social support. *Addison-Wesley Series on Occupational Stress*.

House, J. S., Landis, K. R., & Umberson, D. (1988)a. Social relationships and health. *Science, 241*(4865), 540-545.

House, J. S., Umberson, D., & Landis, K. R. (1988)b. Structures and processes of social support. *Annual review of sociology, 14*(1), 293-318.

Hughes, M. E., Waite, L. J., Hawkley, L. C., & Cacioppo, J. T. (2004). A Short Scale for Measuring Loneliness in Large Surveys: Results From Two Population-Based Studies. *Research on Aging, 26*(6), 655-672. doi:10.1177/0164027504268574

Jacelon, C. S. (2007). Older adults' participation in research. *Nurse Res, 14*(4), 64-73. doi:10.7748/nr2007.07.14.4.64.c6044

Jackson, C. H. (2011). Multi-state models for panel data: the msm package for R. *Journal of Statistical Software, 38*(8), 1-29.

Jacqmin-Gadda, H., Fabrigoule, C., Commenges, D., & Dartigues, J.-F. (1997). A 5-year longitudinal study of the Mini-Mental State Examination in normal aging. *American Journal of Epidemiology, 145*(6), 498-506.

Jiang, H. (2015). Emotional and social difficulties of "shidu" parents in relation to their social transition: the case of Wuxi in China. Universitetet i Nordland,

Jones, M., Mishra, G. D., & Dobson, A. (2015). Analytical results in longitudinal studies depended on target of inference and assumed mechanism of attrition. *J Clin Epidemiol, 68*(10), 1165-1175. doi:10.1016/j.jclinepi.2015.03.011

Jones, W. H., Hobbs, S. A., & Hockenbury, D. (1982). Loneliness and social skill deficits. *Journal of personality and social psychology, 42*(4), 682.

Julsing, J. E., Kromhout, D., Geleijnse, J. M., & Giltay, E. J. (2016). Loneliness and all-cause, cardiovascular, and noncardiovascular mortality in older men: the Zutphen Elderly Study. *The American Journal of Geriatric Psychiatry, 24*(6), 475-484.

Jylhä, M. (2004). Old age and loneliness: cross-sectional and longitudinal analyses in the Tampere Longitudinal Study on Aging. *Canadian Journal on Aging/la revue canadienne du vieillissement, 23*(2), 157-168.

Jylhä, M., & Jokela, J. (1990). Individual experiences as cultural–a cross-cultural study on loneliness among the elderly. *Ageing & Society, 10*(3), 295-315.

Kahn, R. L. (1979). Aging and social support. *Aging from birth to death: Interdisciplinary perspectives, 1*, 77-91.

Karazsia, B. T., & Van Dulmen, M. H. (2008). Regression models for count data: Illustrations using longitudinal predictors of childhood injury. *Journal of pediatric psychology, 33*(10), 1076-1084.

Kuiper, J. S., Zuidersma, M., Oude Voshaar, R. C., Zuidema, S. U., van den Heuvel, E. R., Stolk, R. P., & Smidt, N. (2015). Social relationships and risk of dementia: A systematic review and meta-analysis of longitudinal cohort studies. *Ageing Research Reviews, 22*, 39-57. doi:https://doi.org/10.1016/j.arr.2015.04.006

Kurina, L. M., Knutson, K. L., Hawkley, L. C., Cacioppo, J. T., Lauderdale, D. S., & Ober, C. (2011). Loneliness is associated with sleep fragmentation in a communal society. *Sleep, 34*(11), 1519-1526.

Kurland, B. F., Johnson, L. L., Egleston, B. L., & Diehr, P. H. (2009). Longitudinal Data with Follow-up Truncated by Death: Match the Analysis Method to Research Aims. *Statistical science : a review journal of the Institute of Mathematical Statistics, 24*(2), 211. doi:10.1214/09-STS293

Lancu, I., & Olmer, A. (2006). The minimental state examination--an up-to-date review. *Harefuah, 145*(9), 687-690, 701.

Lau, S., & Gruen, G. E. (1992). The social stigma of loneliness: Effect of target person's and perceiver's sex. *Personality and Social Psychology Bulletin, 18*(2), 182-189.

Lauder, W., Sharkey, S., & Mummery, K. (2004). A community survey of loneliness. *Journal of Advanced Nursing, 46*(1), 88-94. doi:doi:10.1111/j.1365-2648.2003.02968.x

Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: self-maintaining and instrumental activities of daily living. *The Gerontologist, 9*(3_Part_1), 179-186.

Leggett, J. (2016). Action in rural Sussex. Retrieved from https://www.ruralsussex.org.uk/opinions/only-the-lonely-britains-loneliness-crisis-and-the-urbanrural-divide/

Liang, K.-Y., & Zeger, S. L. (1986). Longitudinal data analysis using generalized linear models. *Biometrika, 73*(1), 13-22.

Lichtenstein, P., Gatz, M., & Berg, S. (1998). A twin study of mortality after spousal bereavement. *Psychological medicine, 28*(3), 635-643.

Lin, N., & Dean, A. (1984). Social support and depression. *Social Psychiatry, 19*(2), 83-91.

Little, R. J., & Rubin, D. B. (2002). *Statistical analysis with missing data*. New York: Wiley.

Lofvenmark, C., Mattiasson, A. C., Billing, E., & Edner, M. (2009). Perceived loneliness and social support in patients with chronic heart failure. *Eur J Cardiovasc Nurs, 8*(4), 251-258. doi:10.1016/j.ejcnurse.2009.05.001

Lotfi, Y., Mehrkian, S., Moossavi, A., & Faghih-Zadeh, S. (2009). Quality of life improvement in hearing-impaired elderly people after wearing a hearing aid. *Archives of Iranian Medicine (AIM), 12*(4).

Luo, Y., Hawkley, L. C., Waite, L. J., & Cacioppo, J. T. (2012). Loneliness, health, and mortality in old age: a national longitudinal study. *Social science & medicine, 74*(6), 907-914.

Lynn, P. (1996). Weighting for non-response. *Survey and statistical computing*, 205-214.

Mansournia, M. A., & Altman, D. G. (2016). Inverse probability weighting. *Bmj, 352*, i189.

Marangoni, C., & Ickes, W. (1989). Loneliness: A theoretical review with implications for measurement. *Journal of Social and Personal Relationships, 6*(1), 93-128.

Marioni, R. E., van den Hout, A., Valenzuela, M. J., Brayne, C., & Matthews, F. E. (2012). Active cognitive lifestyle associates with cognitive recovery and a reduced risk of cognitive decline. *Journal of Alzheimer's Disease, 28*(1), 223-230.

Martin, P., Kliegel, M., Rott, C., Poon, L. W., & Johnson, M. A. (2008). Age differences and changes of coping behavior in three age groups: Findings from the Georgia Centenarian Study. *The International Journal of Aging and Human Development, 66*(2), 97-114.

Masi, C. M., Chen, H.-Y., Hawkley, L. C., & Cacioppo, J. T. (2011). A meta-analysis of interventions to reduce loneliness. *Personality and Social Psychology Review, 15*(3), 219-266.

Matthews, F., Marioni, R., & Brayne, C. (2012). Examining the influence of gender, education, social class and birth cohort on MMSE tracking over time: a population-based prospective cohort study. *BMC Geriatr, 12*(1), 45.

McConnell, H., Pickard, L., Lampard, R., Murphy, M., Wilson, B., & Smallwood, S. (2007). Focus on Families: 2007 Edition, Office for National Statistics (ONS); Palgrave Macmillan.

Meira-Machado, L., de Uña-Álvarez, J., Cadarso-Suárez, C., & Andersen, P. K. (2009). Multi-state models for the analysis of time-to-event data. *Statistical Methods in Medical Research, 18*(2), 195-222.

Mijuskovic, B. L. (1988). Loneliness.

Minister for loneliness appointed to continue Jo Cox's work. (2018). Retrieved from https://www.bbc.com/news/uk-42708507

Moher, D., Liberati, A., Tetzlaff, J., & Altman, D. G. (2010). Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. *International journal of surgery, 8*(5), 336-341.

Molloy, G. J., McGee, H. M., O'neill, D., & Conroy, R. M. (2010). Loneliness and emergency and planned hospitalisation s in a community sample of older adults. *Journal of the American Geriatrics Society, 58*(8), 1538-1541.

Morris, J. N., Howard, E. P., Steel, K., Schreiber, R., Fries, B. E., Lipsitz, L. A., & Goldman, B. (2014). Predicting risk of hospital and emergency department use for home care elderly persons through a secondary analysis of cross-national data. *BMC Health services research, 14*(1), 519.

Newall, N., McArthur, J., & Menec, V. H. (2015). A longitudinal examination of social participation, loneliness, and use of physician and hospital services. *Journal of aging and health, 27*(3), 500-518.

Newall, N. E., Chipperfield, J. G., Bailis, D. S., & Stewart, T. L. (2013). Consequences of loneliness on physical activity and mortality in older adults and the power of positive emotions. *Health Psychol, 32*(8), 921-924. doi:10.1037/a0029413

NHS England. (2016). NHS Five Year Forward View. Retrieved from https://www.england.nhs.uk/

Nicolaisen, M., & Thorsen, K. (2014). Loneliness among men and women–a five-year follow-up study. *Aging & mental health*, *18*(2), 194-206.

Number of monthly active WeChat users from 2nd quarter 2010 to 1st quarter 2018 (in millions). (2018). Retrieved from https://www.statista.com/statistics/255778/number-of-active-wechat-messenger-accounts/

O'Connell, A. A. (2006). *Logistic regression models for ordinal response variables* (No. 146). Sage.

O'Connor, D. W., Pollitt, P. A., Hyde, J. B., Fellows, J. L., Miller, N. D., Brook, C. P. B., & Reiss, B. B. (1989). The reliability and validity of the Mini-Mental State in a British community survey. Journal of psychiatric research, 23(1), 87-96.

O'luanaigh, C., O'connell, H., Chin, A.-V., Hamilton, F., Coen, R., Walsh, C., . . . Lawlor, B. (2012). Loneliness and cognition in older people: the Dublin Healthy Ageing study. *Aging & mental health*, *16*(3), 347-352.

Page, R. M. (1991). Loneliness as a risk factor in adolescent hopelessness. *Journal of Research in Personality, 25*(2), 189-195. doi:https://doi.org/10.1016/0092-6566(91)90014-H

Patterson, A. C., & Veenstra, G. (2010). Loneliness and risk of mortality: A longitudinal investigation in Alameda County, California. *Social science & medicine*, *71*(1), 181-186.

Penninx, B. W., Van Tilburg, T., Kriegsman, D. M., Deeg, D. J., Boeke, A. J. P., & van Eijk, J. T. M. (1997). Effects of social support and personal coping resources on mortality in older age: The Longitudinal Aging Study Amsterdam. *American Journal of Epidemiology*, *146*(6), 510-519.

Perlman, D., & Peplau, L. A. (1981). Toward a social psychology of loneliness. *Personal relationships*, *3*, 31-56.

Peterson, B., & Harrell Jr, F. E. (1990). Partial proportional odds models for ordinal response variables. *Applied statistics*, 205-217.

Pinquart, M., & Sorensen, S. (2001). Influences on Loneliness in Older Adults: A Meta-Analysis. *Basic and Applied Social Psychology*, *23*(4), 245-266. doi:10.1207/S15324834BASP2304_2

Pressman, S. D., Cohen, S., Miller, G. E., Barkin, A., Rabin, B. S., & Treanor, J. J. (2005). Loneliness, social network size, and immune response to influenza vaccination in college freshmen. *Health psychology*, *24*(3), 297.

Radloff, L. S. (1977). The CES-D scale: A self-report depression scale for research in the general population. *Applied psychological measurement, 1*(3), 385-401.

Rico-Uribe, L. A., Caballero, F. F., Martín-María, N., Cabello, M., Ayuso-Mateos, J. L., & Miret, M. (2018). Association of loneliness with all-cause mortality: A meta-analysis. *PloS one, 13*(1), e0190033.

Rook, K. S. (1984). Research on social support, loneliness, and social isolation: Toward an integration. *Review of Personality & Social Psychology*.

Rosengren, A., Orth-Gomer, K., Wedel, H., & Wilhelmsen, L. (1993). Stressful life events, social support, and mortality in men born in 1933. *Bmj, 307*(6912), 1102-1105.

Roth, M., Tym, E., Mountjoy, C., Huppert, F. A., Hendrie, H., Verma, S., & Goddard, R. (1986). CAMDEX. A standardised instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *The British journal of psychiatry, 149*(6), 698-709.

Russell, D., Peplau, L. A., & Cutrona, C. E. (1980). The revised UCLA Loneliness Scale: Concurrent and discriminant validity evidence. *Journal of personality and social psychology, 39*(3), 472.

Russell, D. W. (1996). UCLA Loneliness Scale (Version 3): Reliability, validity, and factor structure. *Journal of personality assessment, 66*(1), 20-40.

Russell, D. W., Cutrona, C. E., de la Mora, A., & Wallace, R. B. (1997). Loneliness and nursing home admission among rural older adults. *Psychol Aging, 12*(4), 574-589.

Sadig, H. (2014). Unknown Eligibility whilst Weighting for Non-response: The Puzzle of who has Died and who is still Alive? *ISER Working Paper Series*, 2014-35.

Sasidharan, L., & Menéndez, M. (2014). Partial proportional odds model—An alternate choice for analyzing pedestrian crash injury severities. *Accident Analysis & Prevention, 72*, 330-340. doi:https://doi.org/10.1016/j.aap.2014.07.025

Schaefer, C., Coyne, J. C., & Lazarus, R. S. (1981). The health-related functions of social support. *Journal of Behavioral Medicine, 4*(4), 381-406.

Schafer, J. L. (1999). Multiple imputation: a primer. *Statistical Methods in Medical Research, 8*(1), 3-15.

Schinka, K. C., van Dulmen, M. H., Mata, A. D., Bossarte, R., & Swahn, M. (2013). Psychosocial predictors and outcomes of loneliness trajectories from childhood to early adolescence. *Journal of Adolescence, 36*(6), 1251-1260.

Scholes, S., Medina, J., Cheshire, H., Cox, K., Hacker, E., & Lessof, C. (2009). Living in the 21st century: Older people in England. The 2006 English longitudinal study of ageing. Technical report.

Seeman, T. E. (1996). Social ties and health: The benefits of social integration. *Annals of Epidemiology, 6*(5), 442-451. doi:https://doi.org/10.1016/S1047-2797(96)00095-6

Shaw, J. G., Farid, M., Noel-Miller, C., Joseph, N., Houser, A., Asch, S. M., . . . Flowers, L. (2017). Social Isolation and Medicare Spending: Among Older Adults, Objective Isolation Increases Expenditures while Loneliness Does Not. *Journal of Aging and Health, 29*(7), 1119-1143. doi:10.1177/0898264317703559

Shiovitz-Ezra, S., & Ayalon, L. (2010). Situational versus chronic loneliness as risk factors for all-cause mortality. *International Psychogeriatrics, 22*(3), 455-462.

Singh, A., & Misra, N. (2009). Loneliness, depression and sociability in old age. *Industrial psychiatry journal, 18*(1), 51.

Smagula, S. F., Stone, K. L., Fabio, A., & Cauley, J. A. (2016). Risk factors for sleep disturbances in older adults: evidence from prospective studies. *Sleep medicine reviews, 25*, 21-30.

Song, Y. (2014). Losing an only child: the one-child policy and elderly care in China. *Reproductive health matters, 22*(43), 113-124.

Spratt, M., Carpenter, J., Sterne, J. A. C., Carlin, J. B., Heron, J., Henderson, J., & Tilling, K. (2010). Strategies for Multiple Imputation in Longitudinal Studies. *American Journal of Epidemiology, 172*(4), 478-487. doi:10.1093/aje/kwq137

Steinbach, U. (1992). Social networks, institutionalization, and mortality among elderly people in the United States. *Journal of Gerontology*, 47(4), S183-S190.

Stek, M. L., Vinkers, D. J., Gussekloo, J., Beekman, A. T., van der Mast, R. C., & Westendorp, R. G. (2005). Is depression in old age fatal only when people feel lonely? *American journal of psychiatry, 162*(1), 178-180.

Steptoe, A., Owen, N., Kunz-Ebrecht, S. R., & Brydon, L. (2004). Loneliness and neuroendocrine, cardiovascular, and inflammatory stress responses in middle-aged men and women. *Psychoneuroendocrinology, 29*(5), 593-611.

Steptoe, A., Shankar, A., Demakakos, P., & Wardle, J. (2013). Social isolation, loneliness, and all-cause mortality in older men and women. *Proceedings of the National Academy of Sciences, 110*(15), 5797-5801.

Stern, Y. (2012). Cognitive reserve in ageing and Alzheimer's disease. *Lancet neurology, 11*(11), 1006-1012. doi:10.1016/S1474-4422(12)70191-6

Sterne, J. A., White, I. R., Carlin, J. B., Spratt, M., Royston, P., Kenward, M. G., . . . Carpenter, J. R. (2009). Multiple imputation for missing data in epidemiological and clinical research: potential and pitfalls. *Bmj, 338*, b2393. doi:10.1136/bmj.b2393

Stewart, M., Craig, D., MacPherson, K., & Alexander, S. (2001). Promoting positive affect and diminishing loneliness of widowed seniors through a support intervention. *Public health nursing, 18*(1), 54-63.

Stickley, A., Koyanagi, A., Koposov, R., Schwab-Stone, M., & Ruchkin, V. (2014). Loneliness and health risk behaviours among Russian and U.S. adolescents: a cross-sectional study. *BMC Public Health, 14*(1), 366. doi:10.1186/1471-2458-14-366

Sugisawa, H., Liang, J., & Liu, X. (1994). Social networks, social support, and mortality among older people in Japan. *Journal of Gerontology, 49*(1), S3-S13.

Taube, E., Kristensson, J., Sandberg, M., Midlov, P., & Jakobsson, U. (2015). Loneliness and health care consumption among older people. *Scand J Caring Sci, 29*(3), 435-443. doi:10.1111/scs.12147

The Campaign to End Loneliness. (2011). Retrieved from https://www.campaigntoendloneliness.org/about-the-campaign/

Therneau, T., Crowson, C., & Atkinson, E. (2013). Using time dependent covariates and time dependent coefficients in the cox model. Red, 2, 1.

Thomas, K. S., Akobundu, U., & Dosa, D. (2015). More than a meal? A randomized control trial comparing the effects of home-delivered meals programs on participants' feelings of loneliness. *Journals of Gerontology Series B: Psychological Sciences and Social Sciences, 71*(6), 1049-1058.

Tian, Q. (2010). Community Care for the Elderly: Comparative Study Based on Welfare Pluralism. East China Normal University Doctoral Dissertation.

Tijhuis, M., De Jong-Gierveld, J., Feskens, E., & Kromhout, D. (1999). Changes in and factors related to loneliness in older men. The Zutphen Elderly Study. *Age Ageing, 28*(5), 491-495.

Tilvis, R. S., Kähönen-Väre, M. H., Jolkkonen, J., Valvanne, J., Pitkala, K. H., & Strandberg, T. E. (2004). Predictors of cognitive decline and mortality of aged people over a 10-year period. *The Journals of Gerontology Series A: Biological Sciences and Medical Sciences, 59*(3), M268-M274.

Tilvis, R. S., Laitala, V., Routasalo, P. E., & Pitkälä, K. H. (2011). Suffering from loneliness indicates significant mortality risk of older people. *Journal of aging research, 2011*.

Titman, A. C. (2009). Computation of the asymptotic null distribution of goodness-of-fit tests for multi-state models. *Lifetime Data Analysis, 15*(4), 519. doi:10.1007/s10985-009-9133-5

Titman, A. C., & Sharples, L. D. (2008). A general goodness-of-fit test for Markov and hidden Markov models. *Statistics in Medicine, 27*(12), 2177-2195.

Townsend, P., & Tunstall, S. (1973). Sociological explanations of the lonely. *The social minority*, 240-266.

Tritt, C., & Duncan, R. D. (1997). Research: The Relationship Between Childhood Bullying and Young Adult Self-Esteem and Loneliness. *The Journal of Humanistic Education and Development, 36*(1), 35-44. doi:doi:10.1002/j.2164-4683.1997.tb00426.x

Tsai, F.-J., Motamed, S., & Rougemont, A. (2013). The protective effect of taking care of grandchildren on elders' mental health? Associations between changing patterns of intergenerational exchanges and the reduction of elders' loneliness and depression between 1993 and 2007 in Taiwan. *BMC Public Health, 13*(1), 567.

Tsai, H.-H., Tsai, Y.-F., Wang, H.-H., Chang, Y.-C., & Chu, H. H. (2010). Videoconference program enhances social support, loneliness, and depressive status of elderly nursing home residents. *Aging and Mental Health, 14*(8), 947-954.

Valtorta, N. K., Kanaan, M., Gilbody, S., & Hanratty, B. (2016). Loneliness, social isolation and social relationships: what are we measuring? A novel framework for classifying and comparing tools. *BMJ Open, 6*(4), e010799.

Valtorta, N. K., Moore, D. C., Barron, L., Stow, D., & Hanratty, B. (2018). Older adults' social relationships and health care utilization: A systematic review. *American Journal of Public Health, 108*(4), e1-e10.

van der Zwet, J., Koelewijn-van Loon, M. S., & van den Akker, M. (2009). Lonely patients in general practice: a call for revealing GPs' emotions? A qualitative study. *Family Practice, 26*(6), 501-509. doi:10.1093/fampra/cmp059

Vanhalst, J., Goossens, L., Luyckx, K., Scholte, R. H., & Engels, R. C. (2013). The development of loneliness from mid-to late adolescence: Trajectory classes, personality traits, and psychosocial functioning. *Journal of Adolescence, 36*(6), 1305-1312.

Victor, C., Grenade, L., & Boldy, D. (2005)a. Measuring loneliness in later life: a comparison of differing measures. *Reviews in Clinical Gerontology, 15*(1), 63-70.

Victor, C. R., Scambler, S. J., Bowling, A., & Bond, J. (2005)b. The prevalence of, and risk factors for, loneliness in later life: a survey of older people in Great Britain. *Ageing & Society, 25*(6), 357-375.

Victor, C. R., & Bowling, A. (2012). A longitudinal analysis of loneliness among older people in Great Britain. *The Journal of Psychology, 146*(3), 313-331.

Victor, C. R., & Yang, K. (2012). The Prevalence of Loneliness Among Adults: A Case Study of the United Kingdom. *The Journal of Psychology, 146*(1-2), 85-104. doi:10.1080/00223980.2011.613875

Warner, D. F., & Adams, S. A. (2016). Physical disability and increased loneliness among married older adults: The role of changing social relations. *Society and Mental Health, 6*(2), 106-128.

Weber, M. (1978). *Economy and society: An outline of interpretive sociology* (Vol. 1): Univ of California Press.

Weiss, R. S. (1973). Loneliness: The experience of emotional and social isolation.

Weiss, R. S. (1974). The provisions of social relationships. *Doing unto others*, 17-26.

Wellman, B., & Leighton, B. (1979). Networks, neighborhoods, and communities: Approaches to the study of the community question. *Urban affairs quarterly, 14*(3), 363-390.

Wells, G., Shea, B., O'connell, D., Petersen, J., Welch, V., Losos, M., & Tugwell, P. (2012). The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Department of Epidemiology and Community Medicine, University of Ottawa, Canada. *University of Ottawa, Canada: Available at: www. ohri. ca/programs/clinical_epidemiology/oxford. asp*.

Wen, M., & Wang, G. (2009). Demographic, psychological, and social environmental factors of loneliness and satisfaction among rural-to-urban migrants in Shanghai, China. *International Journal of Comparative Sociology, 50*(2), 155-182.

Wenger, G. C., & Burholt, V. (2004). Changes in levels of social isolation and loneliness among older people in a rural area: A twenty–year longitudinal study. *Canadian Journal on Aging/la revue canadienne du vieillissement, 23*(2), 115-127.

Wenger, G. C., Davies, R., Shahtahmasebi, S., & Scott, A. (1996). Social isolation and loneliness in old age: review and model refinement. *Ageing & Society, 16*(3), 333-358.

White, I. R., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. *Stat Med, 30*. doi:10.1002/sim.4067

Wiles, J. L., Leibing, A., Guberman, N., Reeve, J., & Allen, R. E. (2012). The meaning of "aging in place" to older people. *The Gerontologist, 52*(3), 357-366.

Wilson, R. S., Krueger, K. R., Arnold, S. E., Schneider, J. A., Kelly, J. F., Barnes, L. L., . . . Bennett, D. A. (2007). Loneliness and risk of Alzheimer disease. *Archives of general psychiatry, 64*(2), 234-240.

World Health Organization. (2009). World Health Statistics. Retrieved from http://www.who.int/whosis/whostat/EN_WHS09_Full.pdf?ua=1

World Health Organization. (2015). World report on ageing and health. Retrieved from http://www.who.int/ageing/events/world-report-2015-launch/en/

Wright, K. B. (2005). Researching Internet-Based Populations: Advantages and Disadvantages of Online Survey Research, Online Questionnaire Authoring Software Packages, and Web Survey Services. *Journal of Computer-Mediated*

Communication, 10(3), JCMC1034-JCMC1034. doi:10.1111/j.1083-6101.2005.tb00259.x

Xu, S., Ross, C., Raebel, M. A., Shetterly, S., Blanchette, C., & Smith, D. (2010). Use of stabilized inverse propensity scores as weights to directly estimate relative risk and its confidence intervals. *Value in Health*, 13(2), 273-277.

Yang, K., & Victor, C. (2011). Age and loneliness in 25 European nations. *Ageing & Society, 31*(8), 1368-1388.

Yeh, S.-C. J., & Liu, Y.-Y. (2003). Influence of social support on cognitive function in the elderly. *BMC Health services research, 3*(1), 9.

Zhou, J., & Walker, A. (2016). The need for community care among older people in China. *Ageing & Society, 36*(6), 1312-1332.